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PAPILLARY CARCINOMA OF THE RENAL PELVIS

Diagnosis and Treatment

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NO more than 10 years ago papillary carcinoma of the renal pelvis was looked upon as a very rare lesion. But during the past decade an increasingly large number of these renal growths has been put on record, so that their occurrence can no longer be regarded as uncommon. It is probable that this increase in incidence is more apparent than real. The employment of improved methods of urologic diagnosis has made it possible to detect the existence of these growths in the living unoperated upon patient, and this in turn, has increased our knowledge of the pathological and clinical manifestations of all types of renal tumors, papillary epithelioma among them.

Up to the beginning of the present century the great majority of these tumors were recognized only at autopsy. The classic monograph of Albarran and Imbert, published in 1903, wherein the literature up to that date was thoroughly reviewed, listed but 42 tumors of the renal pelvis in a total of 585 renal tumors of all kinds. Of these but 18 were of the papillary type. Statistics of the Mayo Clinic from 1905 to 1922 showed but 13 renal pelvic tumors, of which but 8 were of the papillary type (7). In 1927 when Hunt made a further report from this same clinic, the number of papillary tumors of the renal pelvis had risen to 15. In 1933, Kimball and Ferris from our clinic at the Brady Foundation collected 72 cases from literature, to which they added 2 more seen in their own service. In the 8 years which have elapsed since their paper was written, we have seen 3 cases of benign renal pelvic papilloma, and 4 malignant growths of the same nature. Writing in 1939, F. P. Johnson placed the incidence of papillary carcinoma of the renal pelvis at 4.9 per cent of all tumors of the kidney.

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ETIOLOGY

Though we have no positive evidence concerning the origin of papillary carcinoma in the pelvis of the kidney, there is a strong probability that long continued irritation and inflammation may have some influence in its production. Stone, however, has never been put forward as a primary etiological factor; though it is occasionally mentioned, the coincidence is not frequent enough to permit any definite conclusions to be drawn. It seems more likely that the calculi were produced by the same conditions which favored the papillary growth. Scholl quotes Orth as having expressed the opinion that papillary or villous inflammation may be the initial form of what later becomes a papillary growth—that it merges into it and cannot be histologically dis-

tinguished from true papillary tumor. When the apparently uninvolved mucosa and submucosa bordering on the papillomatous area were microscopically examined, small villous processes, apparently inflammatory, were often found which were of a distinctly different type from the villous processes usually seen in connection with calculus formation of inflammation which has been confined to the epithelial layer. But at times the papillary processes will be found to involve the submucosa as well. When this occurs the submucosa will almost always show inflammatory reaction by the growth of fibrous tissue, attenuation of the walls of the blood vessels, granulation tissue formation, and the presence of round and plasma cells. The cellular tissue proliferation eventually leading to papillary carcinoma may arise from a regenerative fibrosis which takes place after inflammatory injury to the epithelium, or walls of the blood vessels. An excessive overgrowth of epithelium under these circumstances might produce such formations.

PATHOLOGY

Pathological reports vary considerably, probably because different investigators see the growths in all stages of development. One that was "only moderately rapidly growing" with a "fairly mature type of cell," seen by Hunt and Bennett, had the pelvic mucosa covered by a stratified layer of epithelium of irregular contour because of the many branched and anastomosing stalks which projected into the lumen of the renal pelvis. The epithelium was supported by a very delicate stroma which showed no tendency toward infiltration of the wall. Individually, the cells were large, their cytoplasm abundant, and their vesicular nuclein rather large. The cells of the basal layer were cuboid, but superficially more were of fusiform or spindle shape. Many perivascular lymphoid deposits were seen in the hypertrophied fibromuscular wall.

The growths are most often found at the ureteropelvic junction, and for this reason the ureter is likely to be invaded very shortly. If growth is at all vigorous, the renal pelvis is rapidly filled, and the ureter may be involved by direct extension, or by transplants carried down in the normal process of urine excretion.

Henry Wade has said that "papilloma of the renal pelvis may be regarded as an innocent newgrowth possessing a very high degree of potential malignancy." He describes it as growing from the lining membrane of the renal pelvis or calyces into the lumen of the channel without invading the renal parenchyma. The delicate branching villi consist of a central core of connective tissue cells with large blood vessels, both covered by transitional epithelium. When malignancy begins in a previously benign growth, the change will first be noticeable in the cells at the base, and for a long time thereafter examination of the peripheral villi will show them still without any malignant characteristics. This emphasizes the importance of taking biopsy specimens from the full height of the growth, or better still obtaining more than one specimen from different portions. Only thus can the true nature of a neoplasm be recognized.

SYMPTOMS

The single symptom characteristic of all cases is intermittent hematuria, and this is common to so many other lesions of the upper urinary tract that it cannot be relied on to indicate that a pelvic tumor is present. Often the appearance of blood in the urine has been noted by the patient at intervals during several years previously. There is no pain and the patients are, as a rule, in good physical condition, until such time as the growth has advanced far enough to obstruct the outflow of urine, or to produce pressure symptoms, and when these symptoms are in evidence, the growth is usually too far advanced to permit adequate treatment. Therefore, the appearance of blood in the urine should *always* be looked upon as a grave matter, and every means available be put into use to discover its source. If this were a never varying rule of all physicians, renal neoplasms would be recognized much earlier than is now the case, and many lives, now being needlessly sacrificed, would be saved.

DIAGNOSIS

The history seldom contains anything more than the occasional occurrence of painless hematuria. A marked increase in the amount

of blood is usually what brings the patient for urological examination. The growth seldom enlarges the kidney enough to make its palpation possible. When the cystoscope is brought into use it is not uncommon to find a secondary papilloma—or a group of many—in the bladder, and the examiner may be satisfied that this is the source of the bleeding and investigate no further. The necessity for *complete* urological examination is thus emphasized. If ureteral catheters are passed during cystoscopy the affected side *may* yield blood-stained urine, but this is by no means the rule. If the instrumentation is skillfully done, the impact of the catheter upon the villi of the growth often causes no hemorrhage, and if a plain x-ray film be made while the catheter is still in the ureter, it is not likely to show anything abnormal. Even when an opaque medium is injected it may not be possible to detect any change from the normal outline of the pelvis and calyces. Wade suggests, however, that a very careful inspection of such an x-ray film will show that "the density of the opacity within the pelvis is seen to vary, and thus the shadow outline of the growth within the cavity is obtained. A delicate soft photograph is required to demonstrate this appearance, and

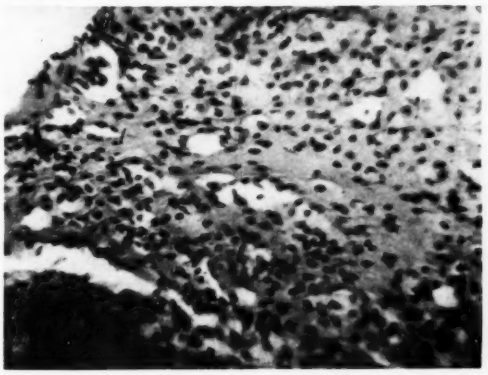

Fig. 2. Diagnosis by aspiration: photomicrograph of material aspirated by method of Vincent Archer (case of Dr. Samuel A. Vest).

Fig. 3.

Fig. 3. Excretory pyelogram showing the superior calyx pushed downward, suggesting a tumor mass. Impression heightened by definite defect in pelvic outline: Inferior calyx, though within normal limits, is displaced slightly downward, a factor also suggesting the presence of mass pressure from above.

Fig. 4.

Fig. 4. Retrograde pyelogram, with findings practically identical with those shown in Figure 3.

Fig. 5. Kidney injected after nephrectomy. Note how calyces are pushed downward by the tumor mass.

it is well worth while to repeat the injection to confirm this observation if doubt exists, as the appearance is dependent on the density of the tumor being less than that of the pyelographic medium, and thus the diagnosis rests on the demonstration of a slight alteration in the density of the shadow." But if a filling defect can be recognized, the diagnosis can usually be established, when taken in connection with the previous findings. Differentiation from renal tuberculosis or stone will, however, at times prove troublesome.

Diagnosis by aspiration. In one of his last publications, the late John Roberts Caulk suggested that in the diagnosis of pelvic neoplasms "the microscopic examination of bits of tissue in the urine or examination of washings from the renal pelvis with recovery of tumor cells will prove of great assistance." This idea has been elaborated by Dr. Vincent Archer, roentgenologist at the University of Virginia Hospital. In a case seen in the department of urology at that institution, Dr. Kirby, after making the pyelogram, left the catheter in the pelvis where a papillary growth was suspected, and "forcibly aspirated" material for microscopic study. The cells thus secured were many of them "obviously malignant" and "there was even a suggestion of papillary growth"—most valuable confirmatory evidence for the pyelographic diagnosis (Fig. 2).

Excretion urography. For the diagnosis of renal pelvic growths, excretion urography is very seldom as satisfactory as the retrograde method. This is because the function of the affected kidney is usually so reduced that it cannot excrete enough of the contrast medium to produce clear roentgenograms. Therefore, unless it be positively contraindicated, the older method should always be used. In the case herein reported both methods were employed, but because function in the affected kidney had remained remarkably good there is practically no difference between them (Figs. 2 and 3).

PROGNOSIS

The outlook for the patient proved to be harboring a papillary growth of the renal pelvis is hedged about with many "ifs" and "buts." So far, no rule has been laid down by which we may even attempt to estimate the chance of recurrence after surgical removal, nor have we discovered any law governing the frequency with which benign lesions may become malignant. But as a general rule, recurrence is likely, and untreated benign papilloma will eventually become malignant. Therefore, all papillomas of the renal pelvis should be looked upon as potentially, if not actually, malignant and should be dealt with accordingly.

TREATMENT

In general, tumors of the renal pelvis are classed as "radioresistant," and the majority of urologists consider complete surgical removal of the affected kidney to be the only safe course. Caulk and some others have advocated preliminary roentgen therapy, believing that there would be less danger of dis-

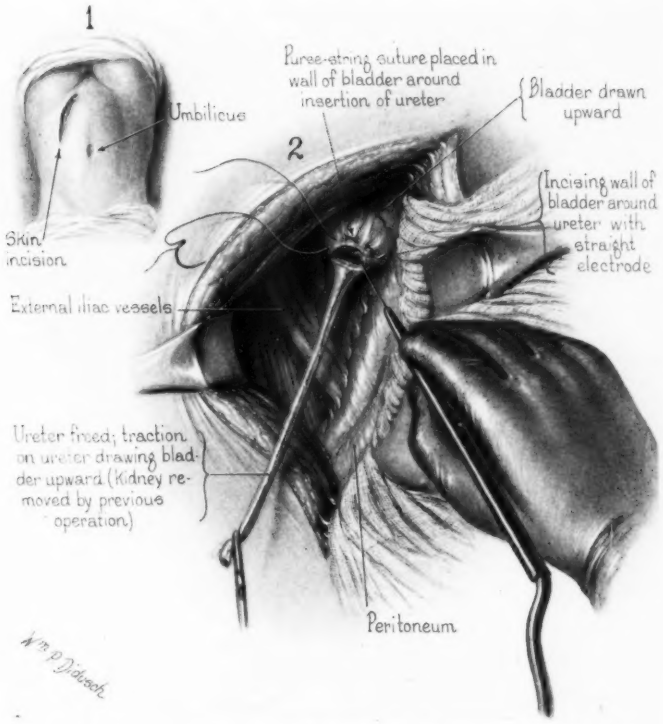
1
Purse-string suture placed in wall of bladder around insertion of ureter
Bladder drawn upward
Umbilicus
2
Incising wall of bladder around ureter with straight electrode
Skin incision
External iliac vessels
Ureter freed; traction on ureter drawing bladder upward (Kidney removed by previous operation)
Peritoneum

Fig. 8. Left ureterectomy, secondary to left nephrectomy. *1*, Skin incision. *2*, Ureter freed and withdrawn from wound; traction exerted on ureter draws bladder upward. Purse-string suture placed in bladder wall, encircling insertion of left ureter. With a straight-wire electrode, bladder wall is incised, a cuff of healthy mucosa being left attached to excised ureter.

semination of the tumor cells when nephrectomy was carried out. Postoperative x-ray and the implantation of radon seeds have likewise been advocated and practiced. But Waters, of the Brady Urological Institute of Johns Hopkins University, who has had an exceptionally wide experience in urological roentgenography, has pointed out that as all renal pelvic growths tend toward the squamous cell type, in that they are not derived from transitional epithelium, they are inevitably resistant to radiotherapy and cannot be expected to show as good results from this therapy as do the larger cortical growths of the kidney.

Because metastasis or extension to the ureter is so common an occurrence in malignant pelvic growths, complete nephroureterectomy is, in my opinion, the only safe course to pursue. This is often done at a single operation, because of fear that tumor cells may be disseminated by the first—incomplete—step of the procedure. Pathological investigation has shown that malignancy readily spreads by implantation to the ureteral mucosa, often reaching the bladder, where secondary growths may appear around the ureteral meatus.

This same danger makes simple nephrectomy an inadequate measure for dealing with these pelvic growths. Early in the present century surgeons began not only removing the kidney and upper third of the ureter, but extirpating the entire upper urinary tract, including a "cuff" of vesical mucosa surrounding the meatus of the operated ureter. But, as J. A. C. Colston has said, "This operation

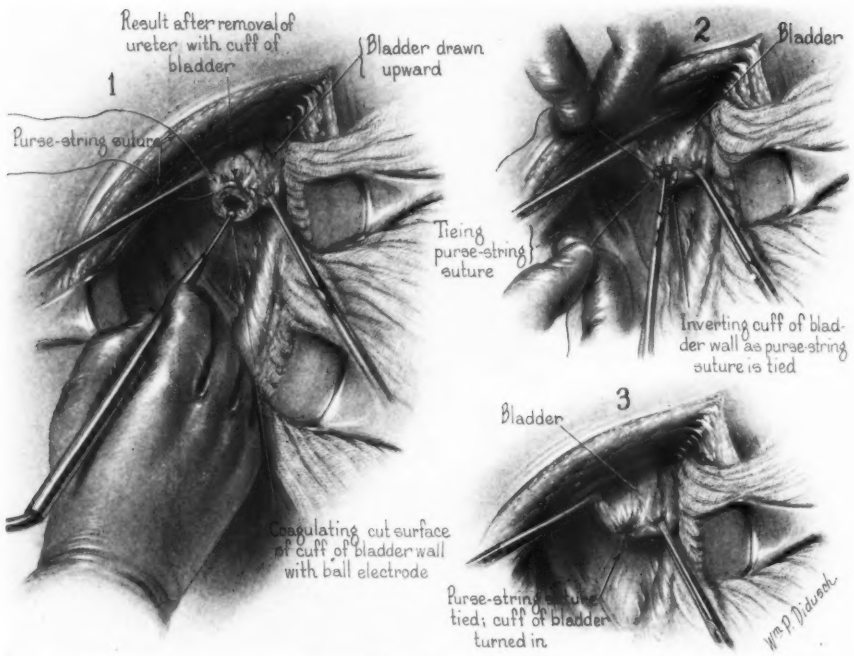
Result after removal of ureter with cuff of bladder
Bladder drawn upward
1
Purse-string suture
2
Bladder
Tieing purse-string suture
Inverting cuff of bladder wall as purse-string suture is tied
3
Bladder
Coagulating cut surface of cuff of bladder wall with ball electrode
Purse-string suture tied; cuff of bladder turned in
Wm P. Didusch

Fig. 9. Left ureterectomy, secondary to left nephrectomy. *1*, Ureter removed; traction on bladder by means of Allis clamps; coagulation of cut edge of bladder by ball-electrode. *2*, Tying of purse-string suture inverts cut edges into bladder cavity. *3*, Tying of purse-string suture has effectively closed opening in bladder wall left by removal of ureter.

is a rather formidable procedure, is taxing on many patients and, particularly in obese individuals, satisfactory exposure of the lower end of the ureter as it enters the bladder, may present serious technical difficulties. It has further been found that the suture in the bladder wall may slough leading to troublesome urinary fistulae, and the possibility of deep-seated infection in a locality which is hard to drain." Colston conceived the idea of using the electrocautery knife for the excision, thus minimizing the danger of malignant transplants. Also this method took less time, and was better borne by much enfeebled patients.

CASE REPORT

A woman, 41 years old, entered the James Buchanan Brady Foundation for Urology on March 8, 1940. She gave a history of painless hematuria at intervals of about 48 hours for 2 weeks past; no other urological symptoms. The physical examination revealed nothing abnormal, and no red blood cells appeared in the urine at this time. Cystoscopy was done with the flat plate and bilateral pyelograms and pyeloureterograms, giving an impression of tumor at the superior pole of the left kidney. Excretory ureterograms obtained 3 days later showed the same morphology as had the retrograde investigation. A mass in the upper pole of the left kidney seemed to be pushing the middle group of calyces downward (Fig. 4). Upon these findings a diagnosis of tumor of the left kidney was made, and left nephrectomy carried out. Convalescence was uneventful, the patient being discharged on the sixteenth postoperative day, to return later for ureterectomy. The pathological diagnosis was papillary carcinoma of the renal pelvis. The sectioned kidney is shown in the colored plate (Fig. 1). The papillomatous mass occupied the upper two-thirds of the left pelvis, as well as the calyces in the upper part of the kidney. The papillae were flattened and the epithelium of the calyces replaced by tumor growth (Fig. 6). A smooth lined cyst approximately 2 millimeters in diameter occupied the lower pole of the left kidney. The remainder of the left kidney was entirely normal (Fig. 7). The 4 centimeter length of ureter which had been removed with the kidney showed no evidence of carcinoma, though the subepithelial tis-

sue was edematous and infiltrated with leucocytes, as were the muscles also. Numerous hemorrhages were in evidence in the wall and in the submucosa.

On April 23, 1940, 6 weeks after the first operation, the patient re-entered the Brady Foundation for secondary ureterectomy. There had been no urinary symptoms during the interval, and the physical and laboratory findings were essentially negative. Under avertin and gas oxygen anesthesia incision was made along the outer border of the left rectus muscle, incurving toward the median line (Fig. 8, *1*), exposing the ureter, which was freed and drawn from the wound. Traction was exerted upon the ureter in such a manner as to draw the bladder upward. A purse-string suture was run around the bladder at its vesical insertion. By use of a straight-wire electrode the ureter was then freed from the bladder wall, and a cuff of healthy tissue was left completely encircling it (Fig. 8, *2*).

After removal of the ureter, traction was maintained upon the bladder by means of Allis clamps. The cut edge above the purse-string suture was carefully coagulated with the ball electrode to prevent any possible dissemination of tumor cells (Fig. 9, *1*). The suture was then gradually drawn together, everting the cut edges within the bladder cavity as the orifice left by the ureter's removal was obliterated (Fig. 9, *2*). In Figure 9, *3*, may be seen the outside appearance of the bladder after the purse-string suture was tied. This procedure, while following the technique of Colston quite closely, differs in that he merely coagulated the stump of the ureter where it had been cut off on the external surface of the bladder wall. He did not remove a precautionary "cuff" of healthy vesical mucosa, nor did he make use of the purse-string suture to draw up and evert the opening in the bladder wall.

Pathological report on the ureter. Sections taken at 1 centimeter intervals throughout the length of the excised ureter gave no evidence of carcinoma, though in one section there was a small papillary projection of the epithelium. Throughout the subepithelial tissue there was an occasional area of infiltration, and still more rarely, an invasion by polymorphonuclear leucocytes. The ureter was hyperemic throughout, with several areas of frank hemorrhage, but nowhere was malignancy in evidence.

Prognosis in this case is very good, as the patient, so far, remains in excellent condition. Though Ewing states that metastases are often observed in adjoining nodes or in the adrenal, in the peritoneum or other neighboring structures, careful search has, in this case, revealed nothing of the kind. We believe, however, that the precaution of secondary complete removal of the ureter was well taken, even though it proved *not* to contain any malignant extension of the pelvic growth. The well known tendency of "benign" papillomas to become malignant, and the evidence of a pronounced chronic ureteritis give ground for the assumption that, had the ureter been left *in situ*, malignancy would eventually have occurred.

SUMMARY

Papillary carcinoma of the renal pelvis is a relatively uncommon form of neoplasm, though a steadily increasing incidence would seem to be indicated by the number of reports concerning it which have recently appeared in medical literature. This is due, however, not so much to actual increase in the number of cases, as to improvements in urological diagnostic methods, which permit more frequent recognition of the lesion.

The embryonic relationship between the ureter and the renal pelvis is much closer than the ureter's structural affinity to the kidney proper. Therefore, neoplastic growth in the renal pelvis extends rather to the ureter than to the renal cortex.

For this reason, the hope of permanent removal of the disease lies in surgical extirpation of both kidney and ureter, even if no active proliferation can be detected in the ureteral mucosa. Complete nephroureterectomy is the only answer to the surgical problem. This may be done in either one or two stages.

A case report is presented in which a modification of Colston's procedure is described.

The results achieved in this case give ground for the belief that no time should be wasted in the application of x-ray therapy. Coutard's method of fractional dosage was attempted, but the patient proved unable to endure it. We have no reason to think that her present condition would be in any way better had the full dosage demanded by this therapy been administered.

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THE GASTROINTESTINAL TRACT IN HYPERTHYROIDISM

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DIGESTIVE disturbances in hyperthyroidism are often so overshadowed by cardiovascular, neuromuscular, or ocular manifestations that they are not given proper consideration. Hyperthyroidism may not be recognized when the symptoms are chiefly gastrointestinal. Frequently in this type of thyrotoxicosis, as exemplified by a series of 34 cases reported by Verbrycke, there is little or no clinical evidence of thyroid enlargement. Only when the physician has been educated to the causal relationship between hyperthyroidism and digestive disturbances is the basal metabolic reading requested and the diagnosis established.

As early as 1896 Moebius wrote of diarrhea as an important symptom of Basedow's disease. He regarded the diarrhea as an attempt on the part of the body to eliminate a toxin with which it was overladen. Many other ingenious but equally unproved explanations for the diarrhea of thyrotoxicosis have been advanced (16, 22).

Increase in appetite, nausea and vomiting, and even abdominal pain may be manifestations of hyperthyroidism. Although loss of weight may be dependent in part upon gastrointestinal disturbances, it should not be considered primarily a gastrointestinal symptom. It is more directly related to an increase in metabolism and to the effects of a vitamin B complex deficiency (17, 21, 43).

An idea as to the frequency of occurrence of these gastrointestinal symptoms may be obtained from the following statistics. Verbrycke, in his 34 cases of hyperthyroidism with predominant gastrointestinal symptoms, found abdominal pain as a chief complaint in 16, nausea and vomiting in 9, gas in 5, and diarrhea in 3. Shirer found diarrhea in 14 per cent of 42 patients studied, constipation in 31 per cent, and normal bowel habits in 55 per cent. Tinker (51) reported digestive disturbances in 1,415 of 4,127 cases of goiter. Persistent diarrhea was present in 10 per cent of these patients, nausea and vomiting in 10 per cent.

Although the occurrence of gastrointestinal symptoms in hyperthyroidism is an established fact, the underlying disturbances in gastrointestinal physiology are too often only a matter of conjecture. Any study of these fundamental changes must of necessity be divided into two main groups: first, a study of secretory activity; second, a study of motor activity.

GASTRIC SECRETION

In 1904 Miesowicz reported the absence of hydrochloric acid in the gastrointestinal secretions of 7 patients with Basedow's disease examined both in a fasting state and after a protein test meal. Since that time many authors have reported similar findings.

Wolpe studied 16 cases of Basedow's disease and found hypochylia or achylia in a majority. He found the greatest reduction in free acid in advanced cases. Badylkes obtained similar results on administering dried thyroid to normal individuals. In a majority of the cases gastric secretion was diminished both in amount and in free and total acid content. These were the individuals with the most pronounced reaction to the thyroid medication, as judged chiefly by its effect on the cardiovascular system. In those with a mild reaction, gastric secretion was increased in amount.

Lerman and Means (29) found anacidity in 38 per cent of a group of 50 patients with exophthalmic goiter. They found that the achlorhydria became more frequent not only with increase in the basal metabolic rate but also with increase in age and severity of anemia. Moll and Scott (40), Wilkinson, and

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Schwanke, all found a high incidence of achlorhydria in hyperthyroidism but related it to duration rather than to severity of the disease. On the other hand, Alfred Brown found a greater percentage of achlorhydria in cases of short duration. Berryhill and Williams found achlorhydria in 69 per cent of 35 patients with exophthalmic goiter and 67 per cent of 15 patients with toxic adenomas. They found no correlation with age, duration of the disease, or metabolic rate. Leist found achylia in 2 and anacidity in 5 of 8 cases studied, even in the presence of concomitant hyperchloremia. He believed that these abnormalities in gastric secretion were related to the low protein content of the blood serum.

Lewit found hypoacidity in 4 and achylia in 5 of 10 patients with classical Basedow's disease. In addition he studied 17 cases of this disease which had come to autopsy. Atrophy of the gastric mucosa was present in 10 cases. On the basis of these findings Lewit postulated a form of achylia dependent on organic changes as well as one dependent on functional changes. Whatever the underlying cause for these disturbances in gastric secretion may be, the process is certainly not irreversible. In Berryhill and Williams' series, 73 per cent of the hyperthyroid cases with an initial achlorhydria showed, after treatment, a return of the gastric secretion to within normal limits. Wilkinson found that 22 of 25 cases of hyperthyroidism with a preoperative achlorhydria had free acid in the gastric contents when examined 3 months after operation.

Another group of investigators (11, 15, 32, 39, 45) did not find a high incidence of achlorhydria in the cases of hyperthyroidism studied by them. Normal values for free acid were obtained from the gastric secretions of patients with toxic adenomas studied by Moll and Scott (40). In 11 cases of *forme fruste* reported by Lewit the findings were similar. Still another group has reported high gastric acidity in thyrotoxic states (1, 7, 32, 34, 41, 45). Most cases of Basedow's disease showed hyperacidity in Boenheim's series, especially the early cases. Neilson found hyperacidity an early sign of hyperthyroidism. Badylkes found this increase only in the weak reactor, and Boenheim only after a special test meal and not after the Boas-Ewald meal. Maranon reported hyperchlorhydria in the "vagotonic form of hyperthyroidism" but not in the true Basedow's disease.

Experimental work in this field has yielded equally confusing results. Hardt, Truesdell, Chang and Sloan, all reported a decrease in gastric acid secretion in Pavlov pouch dogs which were fed thyroid substance. Moll and Flint (39) fed thyroid to 4 dogs with Janeway fistulas. They found achlorhydria in 2, slight hypochlorhydria in 1, and increase in acid in 1. Lewit observed an increase in the volume but no change in the acidity of postprandial gastric secretion in Pavlov pouch dogs after the administration of thyroidin.

Although this review of the literature on gastric secretion in hyperthyroidism discloses many apparent discrepancies, we have at the same time received indications of certain factors which may explain in part this confusion of results. Friedman, with the work of Eppinger and Hess as a background, has postulated the presence of both sympathetic and vagal products in thyroid secretion. He has suggested that the effect on gastric secretion depends upon which fraction predominates. The severity of the thyroid intoxication, the duration of the disease, or the type of goiter may be modifying factors in the gastric secretory effects of hyperthyroidism.

There has been no standardization of the technique for gastric analyses through these many studies. Every conceivable type of test meal has been used; single and fractional specimens have been taken at varying time intervals; histamine was administered to some and not to others. Of significance in this connection are the observations of Eggleston (6) and of Bockus, Bank, and Willard. The former noted that the incidence of achlorhydria was twice as great by the single extraction as by the fractional method. The latter group went a step further to demonstrate that after histamine only 53 per cent of those showing achlorhydria with the Rehfuss fractional method failed to secrete acid.

Finally it is only in comparatively recent years that well controlled series of gastric analyses in normal patients have been available as standards of comparison (5, 6, 27, 30,

Fig. 1a.

Fig. 1b.

Fig. 1c.

Fig. 1. Hyperthyroid patient No. 6, (preoperative). a, An orthotonic stomach with very prominent gastric rugae. Emptying time, 5 hours and 30 minutes. b and c, Four plus small intestinal tone with a fine herringbone pattern. Note the transverse position of the upper jejunal loops which we believe is indicative of shortening. The barium reached the cecum in less than 1 hour.

50). As a result of these studies in normals, many physiological factors which definitely influence gastric secretion have been discovered. Achlorhydria increases with age; its incidence is higher in females. A direct relationship has been found between the degree of gastric acidity and the physical fitness of the patient. Acidity also varied directly with the hemoglobin and red blood cell counts in one study (30).

GASTROINTESTINAL MOTOR ACTIVITY

Experiments performed *in vitro* (16, 23) to test the effect of thyroid preparations on excised intestinal muscle, although interesting, have little direct clinical application. The same may be said of the experiments of Boenheim and Wertenberger on frogs. Before proceeding to a consideration of the experimental work on mammals, we should prepare to evaluate the results in the light of the following findings of Carlson and co-workers (10).

Fig. 2a.

Fig. 2b.

Fig. 2. Same case as shown in Figure 1 (postoperative). a, Gastric rugae are less prominent. Although there apparently is more barium in the stomach at this postoperative examination, the amount given for these studies was always the same. Gastric emptying time was 3 hours and 6 minutes. b and c, Small intestinal tone is now classified as 2 to 3 plus. The pattern is coarse herringbone to "stacked coin" in appearance. The short transverse jejunal loops have disappeared.

Fig. 2c.

Man was more susceptible to thyroid feeding than any of the animals studied. Herbivora were more susceptible than carnivora. No nervousness, tachycardia, or exophthalmos was produced in the laboratory animals. Loss of weight, gastroenteritis, and diarrhea were the most common symptoms in all.

Deusch made window observations on living rabbits and found that thyroid preparations increased the motility of the whole gut without producing spasms or incoordinate movements. Perussé and Rozen studied the movements of the empty stomach in gastric fistula dogs after feeding of thyroid. Small dosages (2.5 grams daily) increased the hunger contractions in 4 of 5 dogs. Results with larger dosages were somewhat equivocal.

Fetter and Carlson (20) with balloon recording from the stomach and fluoroscopic observation of the intestines studied the effect of thyroid substance on the gastrointestinal

Fig. 3. Hyperthyroid patient No. 10 (preoperative). Very prominent gastric rugae as viewed in silhouette along the greater curvature at *a*.

tract of 6 dogs. Increased gastric motility and periods of increased tonus were observed in all dogs. As long as 2 months after the feeding of thyroid was stopped 4 of the dogs had not yet returned to normal as regards gastric motility. In 5 of the 6 dogs the stomach emptying time was shortened and the barium reached the colon earlier than in the normal. Barium remained in the colon the normal length of time in all but 1 dog. These investigators discussed several theories to explain this thyroid action, but felt that none was satisfactory. However, in a later set of experiments, Fetter, Barron, and Carlson (19) were of the opinion that they had proved that this thyroid effect was not due to an influence of the thyroid hormone on the gastrointestinal vagus mechanism.

Kratinoff studied dogs with chronic gastric and duodenal fistulas. In 4 of 6 dogs an increase of hunger contractions was observed after thyroid feeding. Intensity of effect depended within definite limits on dosage, and a tendency to develop tolerance was observed. The effects on gastric motility produced by a month's thyroid feeding persisted for at least 10 months after feeding was discontinued.

Finally we come to the observations on humans. With one or two possible exceptions these have been incomplete and often conflicting. Lorenzi found gastric digestion speeded up in 6 cases of hyperthyroidism studied by him. Radiological observations on the rupture of a bismuth filled gelatin capsule served as an indicator. McCarrison stated that dilation of the stomach is a frequent accompaniment of Graves' disease. On the other hand, Crotti reported a state of more or less constant spasticity of the stomach as shown by repeated fluoroscopic examinations.

Heimann studied the stomachs of hyperthyroid patients roentgenographically and found no gross abnormality in the gastric silhouette or emptying time. Curschmann making similar studies also found no disturbance in the form or size of the stomach. However, there was rapid gastric emptying in a few of these cases. Mueller (15) called attention to the "waterfall emptying" of the stomach and to the rapid passage of intestinal content in Basedow's disease with and without gastric symptoms.

Deusch administered thyroid preparations intravenously to normal and to hyperthyroid individuals. He found an increase in the tonus of the colon as observed fluoroscopically. Haustral segmentation was increased as well as peristalsis.

Uermoessy and Lukacs studied the gastrointestinal passage time in a group of 24 babies before and after thyroid administration. They used carmine solution as an indicator. In 15 the passage time was shortened and in 9 lengthened. Those babies with the slowest initial time were the ones in which the passage was usually speeded.

One of the most recent and complete works on this subject is by Shirer. He studied gastrointestinal motility in a group of 42 hyperthyroid patients. Observations were made before and repeated 7 to 10 days after thyroidectomy. The patients were given a barium meal and a roentgenogram was taken 3 hours later to discover the position of the head of the barium column. If this was beyond the cecum, he considered the case one of hypermotility. On this basis, 39, or 92.8 per cent, of his patients showed hypermotility before op-

Fig. 4a.

Fig. 4b.

Fig. 4. Hyperthyroid patient No. 2 (preoperative). a, This examination was made 30 minutes after giving the test meal. Barium is in the cecum at *c*. Small intestinal pattern is variable. In the jejunum in the left upper quadrant the pattern is quite fine. The pattern in the ileum was "stacked coin" at *a* and patchy at *b*. b, This film made 35 minutes later shows a relative delay of barium in the ileum with a reversion toward a more normal pattern *a*.

eration. After operation the motility decreased in 76 per cent, increased in 14 per cent, and remained unchanged in 10 per cent.

SUBJECTS AND METHODS

The experimental group is composed of 24 patients with hyperthyroidism. The following criteria were fulfilled in selecting these subjects for study: (1) an unquestioned diagnosis of hyperthyroidism; (2) an initial basal metabolic rate of plus 30 or higher; (3) absence of associated diseases; (4) no previous treatment for the thyrotoxicosis (Exception: a few patients had received minimal iodine or roentgen therapy but not immediately preceding the study).

Twenty-three of the patients had diffuse toxic goiters and 1 had a nodular toxic goiter. In addition to the routine history, physical examination, blood count, and basal metabolic studies, the following special examinations were made: (1) serum protein determinations; (2) gastric analyses; (3) roentgenological studies of the gastrointestinal tract.

The serum protein studies made on this group of hyperthyroid patients have been reported in a previous article by Brown and Mecray (9). These protein values have been used for correlation with some of our gastrointestinal data.

An oatmeal gruel mixture was used as a test meal for gastric analyses. A tube was passed and the fasting content was removed from the stomach. The test meal was then given. A specimen was collected from the stomach after one-half hour and at 15-minute intervals thereafter for a total of 6 specimens. Immediately upon collection of the first and second specimens Topfer's reagent was added to each. If no free hydrochloric acid was present in either specimen, 0.3 cubic centimeter of a 1:1000 solution of histamine acid phosphate was injected subcutaneously before the remaining samples were collected.

Fig. 5. Hyperthyroid patient (preoperative). Gastric rugae are prominent. The stomach required 4 hours and 40 minutes to empty. The barium reached the cecum in 25 minutes and has progressed into the descending colon. The tone of the small intestine is not greatly increased as judged by our criteria.

Fig. 6. Hyperthyroid patient No. 3 (preoperative). An orthotonic type of stomach requiring 6 hours to empty. Upper small intestines show a fine herringbone pattern *c*. Barium reached cecum in 20 minutes and progressed through colon to fill all portions of gastrointestinal tract. Haustral markings *a* and central lumen of colon *b* are both narrow.

Roentgen studies of the gastrointestinal tract were preceded by a fast of 8 hours, usually from 12:00 o'clock midnight to the following morning. No medication was administered during this period. The patient was then given a water-barium meal and frequent fluoroscopic observations and roentgenograms were made throughout the day and often on several succeeding days. The intervals between observations were relatively short during the early hours of the study so that the gastric emptying time and the time required for the head of the barium column to reach the cecum might be accurately determined. In some cases it was necessary to make these observations every 15 minutes; in others with slower motility the interval was lengthened. However, the impossibility of keeping the patients under this strict observation for the long periods involved in determining the emptying time of the small intestine makes these latter determinations less accurate.

In addition to time observations we have attempted a quantitative estimation of the prominence of gastric rugae, the tone and pattern of the small intestine, and the tone of the large intestine. Rugae were classified as normal, prominent, or very prominent. The intestinal tone and pattern were expressed as 1, 2, 3, or 4 plus with 0 as a hypothetical normal or base line. Since we realize that the personal equation influences such observations, we have reviewed the series repeatedly in order to check and recheck the values assigned. By so doing we believe that we have established values which are significant for comparison of the individual with the individual, the preoperative with the postoperative, and the hyperthyroid patients with the control patients.

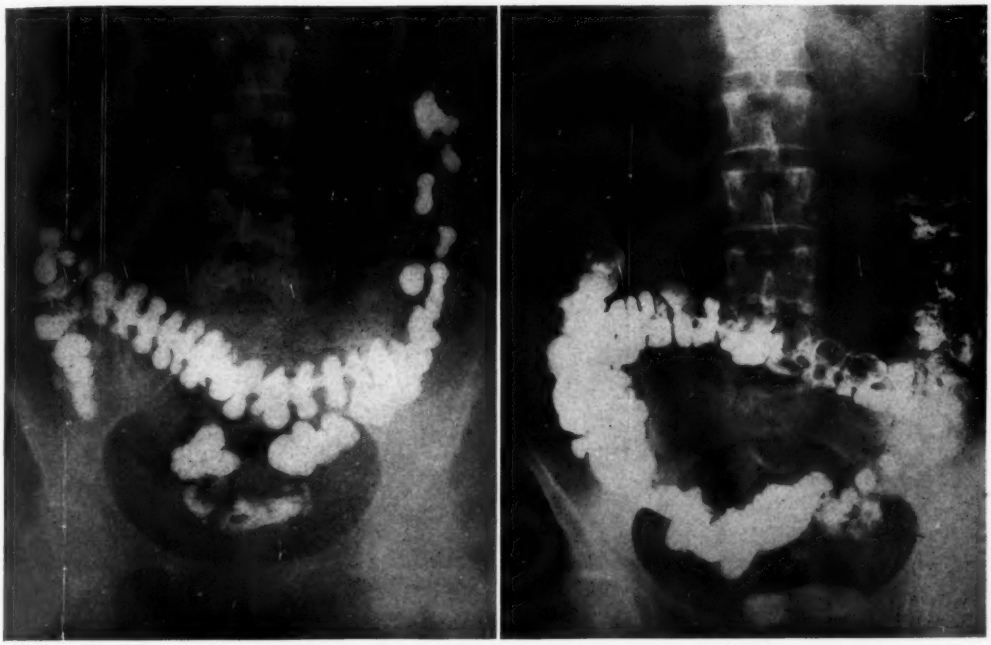

Fig. 7a. Fig. 7b.

Fig. 7. Same case as shown in Figure 6. a, A comparison of preoperative colon studies. b, Postoperative colon studies. Notice the increase in width of haustral markings with what we believe is a decrease in tone after operation.

After completion of the preliminary studies the patients were prepared for operation in the usual fashion. This regimen consisted of bed rest except for 2 hours daily, sedatives, potassium iodide, with high carbohydrate high caloric intake. No vitamins were administered to this group. All the patients with diffuse toxic goiters were subjected to bilateral subtotal thyroidectomy. With few exceptions these operations were performed in one stage. The 1 patient with a nodular goiter required only a hemithyroidectomy. At intervals from 3 to 12 months after operation follow-up studies were made. In 1 case only was there any clinical or basal metabolic evidence of persistence of the thyrotoxicosis. At the time of the follow-up visit roentgen studies of the gastrointestinal tract were repeated exactly as they had been made before operation.

Finally, a control group of 14 composed largely of medical students, doctors, and nurses was subjected to similar roentgenological studies of the stomach and intestines. Individuals were selected who had no gastrointestinal complaints and who had no signs or symptoms to suggest thyroid dysfunction.

EXPERIMENTAL FINDINGS

Gastric secretion. In Table I are presented the data obtained from the gastric analyses in our group of hyperthyroid patients. This material has been analyzed only in respect to achlorhydria. Although the figures for free and total acid are available for all cases studied, we have felt that further to subdivide the group with acid into those with low, normal, or high figures would merely add confusion. Such a subdivision would immediately stimulate arguments as to the normal range of free and total acid, the influence of histamine on such figures, etc.—discussion which we do not propose to consider in this presentation.

However, we wish to make clear our interpretation and usage of the word achlorhydria.

Fig. 8a.

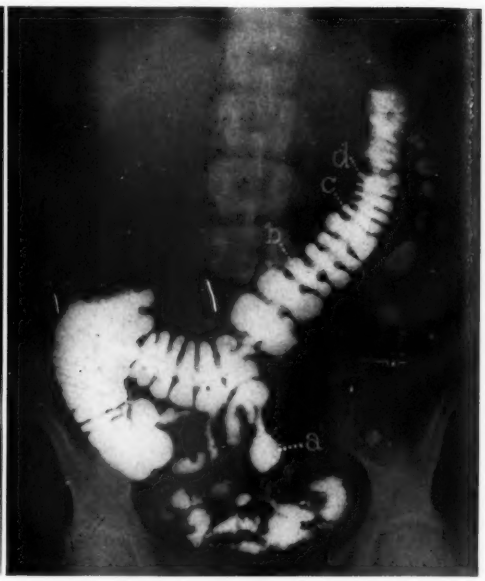

Fig. 8b.

Fig. 8. a, Control case F. Colon of a normal individual which also fits our arbitrary normal as to tone. For comparison with b. b, Hyperthyroid patient, No. 2 (preoperative). This colon has been regarded as hypertonic (2 plus). Note the narrow haustral markings at *b*, *c*, and *d*. The lumen of the colon between the haustra is also somewhat narrowed in comparison with that of the control patient in a.

Achlorhydria means that under certain given experimental conditions an aspirated sample of gastric content contained no titratable free acid. This may have been the result of the suppressed hydrochloric acid secretion but not necessarily so. Hypersecretion of mucus, regurgitation of duodenal content, swallowing of an excess of saliva, or the buffering action of ingested substances, one or all may depress free gastric acid. Much of the gastric analysis work in the literature is meaningless because these facts have not been appreciated.

Thirteen, or 50 per cent, of 26 patients showed no free acid without histamine. Lerman, Pierce, and Brogan (30) found only 13 per cent achlorhydria in a series of 200 normal individuals studied by them. They used an alcohol test meal with histamine. Keefer and Bloomfield reported 1500 consecutive gastric analyses using the Ewald test meal. In those without organic disease anacidity was present in 14.5 per cent. The increased incidence of achlorhydria in our hyperthyroid group as compared to these normals can hardly be questioned even though the technique for gastric analysis was slightly different in each instance.

Unlike many of those whose works have been reviewed, we have not been able to demonstrate a significant relationship between the incidence of achlorhydria and basal metabolic rate, hemoglobin percentage, duration of symptoms, or serum protein level. The age and sex differences are approximately those reported for normal groups. Vanzant and coworkers found in a series of 3,381 normal individuals a greater tendency to achlorhydria in women than men and a definite increase in the incidence of anacidity with increase in age. Lerman, Pierce, and Brogan (30) report an incidence of achlorhydria of 3.6 per cent in those under 30 and of 24.4 per cent in those from 55 to 64 years of age.

Gastrointestinal motor activity. In spite of our review of the literature on the subject, we entered upon this study with few preconceived notions as to what fundamental gastrointesti-

nal changes were to be found in hyperthyroidism. It was, therefore, necessary to outline in advance an all inclusive list of fluoroscopic and roentgenographic observations to be made on each individual studied. For convenience in presentation and analysis this material has been divided into the following groups: (1) type of stomach, tone of stomach, gastric rugae, gastric movements, (2) time stomach started to empty; (3) time stomach was completely empty (gastric emptying time); (4) small intestinal tone and pattern; (5) time barium reached the cecum; (6) time small intestine was completely empty (small intestinal emptying time); (7) tone of colon; (8) time colon was empty (motility of colon).

1. *Type of stomach, tone of stomach, gastric rugae, gastric movements.* The orthotonic type of stomach was found in all individuals studied, both in the hyperthyroid and control groups. It was a J shaped organ which in the erect posture, with the test meal used (5 ounces of barium and 5 ounces of water), showed no tendency for any of its walls to collapse. The transverse diameter of the upper third of the stomach (junction of the fundus and the body) and the transverse diameter of the lower third (junction of the body and pyloric antrum) were approximately the same (Figs. 1a and 3), except when the stomach was very long.

We believe that the type of stomach is determined by anatomical factors, both intrinsic and extrinsic, and do not regard it as an expression of the physiological tone of the organ.

The evaluation of gastric tone in each case has been based upon the manner in which the stomach accepted the first few swallows of the test meal. When the barium progressed in an uninterrupted and regular manner from the esophagus to the pyloric antrum in about 10 seconds, tone was considered normal. In those stomachs which were classified as hypertonic, the swallowed barium was held in the fundus for varying lengths of time and then traveled very slowly toward the antrum. One must be extremely careful not to include in the hypertonic group a cascade type of stomach in which the barium may be trapped in the fundus.

TABLE I.—GASTRIC ANALYSES IN HYPERTHYROID CASES

	No Free HCl—9 cases	Free HCl—17 cases
Average basal metabolic rate..	+65	+61
Average hemoglobin (Sahli) per cent.....	79	79
Average age—years.....	42	33
Sex—		
Males.....	2 (25%)	6 (75%)
Females.....	7 (39%)	11 (61%)
Average duration of symptoms —mos.....	15.2	18.3
Average serum protein—grams per cent.....	6.15	6.16

There were originally 26 patients in our experimental hyperthyroid group. All were studied by gastric analysis. However, 2 of the patients failed to complete their postoperative roentgenograms; thus the group was reduced to 24 for the studies on gastrointestinal motor activity.

The stomach was regarded as hypotonic when the barium traveled faster than normal from the fundus to the antrum. Occasionally the barium moved as though falling through space. Observations on gastric tone were always made before palpation of the abdomen was instituted.

Data were compiled classifying the stomachs of the hyperthyroid patients as to type and tone. Illustrating the point already made that the type of stomach is not a function of its tone, we note that there often was a difference between preoperative and postoperative tone, in any given case, while the type remained the same through the study. On comparing the postoperative with the preoperative it is seen that the change in tone was predominantly downward with a decrease in 10 cases, an increase in 5, and with the remainder of the group unchanged or undetermined. The same data was compiled for the controls. Again the orthotonic type of stomach was found throughout the group. Gastric tone was normal in 9 cases, in 2 the stomach was hypertonic, in 2 hypotonic. Unfortunately, when derived from a sample of this size, the differences in tone observed when the preoperative group is compared with the postoperative group or with the controls are not of sufficient magnitude to be of significance (Methods I and III).[1]

The significance of the prominence of gastric rugae as determined by roentgen examination has not been fully established. In many in-

[1]See appendix for definition of significance and for brief description of methodology. The method number in parenthesis throughout the presentation refers to the corresponding method in the appendix.

TABLE II.—TIME STOMACH STARTED TO EMPTY

	Controls	Hyperthyroid cases		Direction of change
	Time—minutes	Preoperative time—minutes	Postoperative time—minutes	
A	*3	1 *2	*2	Unchanged
B	*2	2 *2	*6	Increased
C	3+	3 *4	Not immediately	?
D	*2	4 *2	*3	Increased
E	*3	5 *9	2+	?
F	5+	6 *5	2+	?
G	*5	7 Almost immediately	*7	Increased
H	*1	8 *Immediately	*3	Increased
I	*3	9 Slight delay	Slight delay	Unchanged
J	*Immediately	10 4+	*12	?
K	*7	11 Delay	3+	?
M	*7	12 Delay	*15	?
N	*5	13 Slight delay	*5	?
O	*5	14 Delay	*5	?
		15 *1	*Immediately	Decreased
		16 4+	13+	?
		17 *2	*4	Increased
		18 *3	*4	Increased
		19 *1	*3	Increased
		20 *5	*3	Decreased
		21 *3	4+	Increased
		22 Almost immediately	*2	Increased
		23 *Immediately	*2	Increased
		24 *2	*9	Increased
Total 43 (12 cases)*		41 (15 cases)*	85 (17 cases)*	
Mean 3.58		2.73	5.00	
Range 0—7		0—9	0—15	

NOTE—Means are only for cases in which time is accurately recorded. Pluses represent an undetermined length of time to be added to the time recorded.

stances increase in prominence may be due to the hypertrophic inflammatory changes of gastritis. In some cases hypertrophy and edema behind pyloric obstruction may explain the picture. In other cases the prominence of mucosal folds may be purely passive and secondary to an increase in gastric tone with contraction of the underlying muscular coats.

Without further explanation of their significance, we present our observations on gastric rugae. The rugae have been described as normal, prominent, or very prominent (Figs. 1a and 3). By a comparison of preoperative studies on the hyperthyroid group with the postoperative studies, it is seen that gastric rugae were less prominent after operation in 11 of the 12 cases which showed a change. The statistical significance (Method I) of these findings is somewhat offset by the fact that 12, or 50 per cent, of the cases showed no change in rugae. Although gastric rugae were definitely less prominent in the patients after operations than before, they were still significantly more prominent than in the controls (Method III). Perhaps we are dealing with a persistent hyperthyroid effect similar to that reported for dogs by Kratinoff and Fetter and Carlson (20).

Although gastric movements were carefully studied under the fluoroscope in all cases of hyperthyroidism, both before and after operation, and in the controls, no significant or uniform differences in type, frequency, or depth of peristaltic movements were found.

2. *Time stomach started to empty.* It has been the experience of one of us (Pendergrass) that the rapidity with which the stomach starts to empty, as determined fluoroscopically, varies greatly from individual to individual and from time to time in the same individual. This is equally true of subjects with or without gastrointestinal pathology. Uncontrollable psychic influences incident to the start of a study, often strange and formidable to the patient, probably have considerable effect on these short time observations. The same is not true of the observations on gastric emptying time, time for the barium to reach the cecum, etc.—observations which extended over a relatively long period of time and upon which the effect of such transient influences becomes minimal.

Because of these considerations we must not overstress the importance of the data presented in this section. Observations on the rapidity with which the stomach started to empty once the barium had reached the pyloric antrum are presented in Table II. In 15 of the hyperthyroid group these observations are accurate enough for comparison of preoperative and postoperative times. In 11 of these 15 cases gastric emptying was initiated more slowly after operation. A comparison of mean times (preoperative 2.73 minutes with

postoperative 5.00 minutes) adds to the significance of the directional change. However, neither the preoperative nor the postoperative mean varies significantly from the control mean (Methods I, III, and IV).

3. *Time stomach was completely empty.* The gastric emptying time has been determined for all cases studied. Frequency of roentgenological observations has been governed in part by a desire to record as accurately as possible the time necessary for the stomach to empty itself completely of the barium meal. In most instances it has been impossible both from the standpoint of x-ray exposure and time consumed to observe the actual endpoint in gastric emptying. Especially was this true when the emptying time was greatly prolonged. The gastric emptying time was then determined by interpolating between observations made on either side of the true end point. We have estimated our maximum error by this method as 30 minutes. The error for the majority of cases was considerably less than this maximum.

The material on gastric emptying time is presented in Table III. Attention must be called to the 3 preoperative hyperthyroid patients whose stomachs were not completely empty at the end of this first day's period of observation. The undetermined additional time required for gastric emptying in these cases is represented by plus signs. These plus signs have been disregarded in our subsequent calculations for the sake of simplicity. This is justifiable since to include them would serve only to increase further the magnitude of the changes which the data demonstrate.

Preoperative and postoperative "gastric emptying times" have been compared for each individual of the hyperthyroid group. Changes of less than 30 minutes were regarded as insignificant because they did not exceed the estimated maximum error of our observations. In 16 cases the stomach emptied more rapidly after operation. In 5 cases the time was unchanged, and in the 3 remaining the stomach emptied more slowly. The significance of this group change toward more rapid gastric emptying can scarcely be questioned (Method I).

Having established this definite directional change we were interested next in studying the magnitude of these observed differences. Groups were compared by using mean values for the gastric emptying times. On an average the stomach took 73 minutes longer to empty in the preoperative hyperthyroid patients than in the postoperative, and 104 minutes longer in the preoperative than in the controls. Both differences are significant (Methods III and IV). This is not true of the difference between the postoperative patients and the controls which was only 32 minutes. The postoperative reversion toward normal in the case of the gastric emptying time was much more complete than for gastric rugae.

Finally, gastric emptying times were analyzed as to variance. A very highly significant difference was found when preoperative hy-

TABLE III.—GASTRIC EMPTYING TIME

	Controls	Hyperthyroid Cases			Direction of change
	Time—minutes		Preoperative time—minutes	Postoperative time—minutes	
A	120	1	120	70	Decreased
B	210	2	180	285	Increased
C	150	3	360	330	Decreased
D	156	4	120	180	Increased
E	120	5	360	375	Unchanged
F	120	6	330	186	Decreased
G	170	7	315	123	Decreased
H	98	8	210	160	Decreased
I	160	9	160	165	Unchanged
J	185	10	150	240	Increased
K	138	11	260	240	Unchanged
M	120	12	450+	240	Decreased
N	140	13	360+	120	Decreased
O	120	14	133	137	Unchanged
		15	240	90	Decreased
		16	360+	240	Decreased
		17	420	180	Decreased
		18	160	105	Decreased
		19	120	65	Decreased
		20	210	120	Decreased
		21	300	120	Decreased
		22	200	135	Decreased
		23	150	165	Unchanged
		24	280	130	Decreased
Mean	143.36		247.83	175.04	

perthyroid patients were compared with controls (Method V). That thyrotoxicosis should produce a varying rather than a uniform delay in gastric emptying, as individual cases are compared, is to be expected in the light of similar and better known effects on other organs. In a group of hyperthyroid patients with approximately the same basal metabolic rate, individual variations in pulse rate, degree of weight loss, severity of eye signs, tremor, etc., are the rule. Why this wider variation persisted after operation in the hyperthyroid group when the mean value for gastric emptying time so closely approached the control value is a question for which we have not found a satisfactory answer.

4. *Small intestinal tone and pattern.* Perhaps the most striking change noted in this study of the gastrointestinal tract in hyperthyroid patients and at the same time the most difficult to evaluate quantitatively were those in small intestinal tone and pattern. It has already been explained that we have chosen to express the degree of change as 1, 2, 3, or 4 plus as compared with an arbitrarily chosen normal. This has been necessary for convenience in analysis and correlation with our quantitative data.

Ordinarily the jejunal loops, as demonstrated roentgenographically, are located in the upper and lower quadrants on the left side. In many of our hyperthyroid patients the jejunal loops occupied a midline position and were transversely placed (Fig. 1). We have interpreted these changes as indicative of small intestinal shortening and believe that this shortening may explain in part the increase in small intestinal motility (5, Time to cecum).

The interpretation of hypertonicity in the small intestine was based upon the apparent decrease in the lumen or transverse diameter of the gut and the types of pattern observed.

Ordinarily (under normal circumstances) there occurs a coarse herringbone pattern in the upper small intestine. In the hyperthyroid patients the pattern was finer and in many instances the herringbone was replaced by an "iron filing" type of pattern (Figs. 1b and c, 6). These changes often were not uniform throughout the entire length of small intestine, and there was occasionally a relative delay of barium in the distal ileum with a reversion toward a more normal pattern (Fig. 4b).

There were no outstanding abnormalities of small intestinal movements noted during the repeated fluoroscopic examinations. Occasional peristaltic rushes were observed and segmentation was often well demonstrated but with no greater frequency than in the controls.

Data were compiled also on small intestinal tone and pattern. A comparison of the hyperthyroid groups shows that after operation there was a predominant change in the direction of decreased tone with a reversion of the pattern toward normal (Fig. 2).

The degree of change is expressed by a difference in means for the groups, computed in terms of pluses. The differences between the preoperative mean and that of the control group may be accepted as highly significant (Methods I, III, and IV). As in the case of gastric rugae, however, the postoperative approach to the control level was not complete.

5. *Time to cecum.* An expression of small intestinal motility, time to cecum is defined as the time elapsing from administration of the meal until the head of the column of barium reached the large intestine. As in determining gastric emptying time, it was seldom possible actually to observe the true end point. Again it was necessary to estimate it by interpolating, in this instance, between observations made before and after the opaque meal entered the cecum. Because of the relatively short times involved, estimations of time to cecum could be made with much greater accuracy than those for gastric emptying time. Our maximum error for time to cecum probably did not exceed 10 minutes.

Data assembled showed that after operation 18 of the 24 hyperthyroid patients required increased time for the barium to reach the cecum. In 2 other cases the postoperative change was in the same direction but did not exceed our estimated maximum error of 10 minutes. In only 4 instances was the time to cecum decreased after operation.

As in many of the preceding sections a significant directional change (Method I) is substantiated by the degree of change determined

by comparison of means. The difference of 40 minutes between the preoperative and postoperative hyperthyroid means and the difference of 60 minutes between the preoperative hyperthyroid mean and that of the controls are both highly significant in themselves. That the postoperative return to normal has been fairly complete is shown by the relatively insignificant difference between the means for this group and the control mean (Methods III and IV).

6. *Time small intestine was completely empty (small intestinal emptying time).* Because of the long periods involved, determination of the time required for the small intestine to empty is in many cases an approximation. Frequently some of the barium still remained in the small intestine at the end of the first day. In 9 of the hyperthyroid cases a comparison of the preoperative and postoperative small intestinal emptying times was impossible. In 5 instances there was no change. In 4 individuals the small intestinal emptying time decreased, and in 6 it increased after operation. This failure to demonstrate a definite change for the group as a whole is not unexpected when we consider that the postoperative decrease in gastric emptying time and the increase in time to cecum tended to balance one another.

The means for the preoperative and postoperative hyperthyroid groups and for the controls have been computed; only those cases were used whose small intestinal emptying times were accurately determined. These means obviously do not differ significantly.

7. *Tone of colon.* Adopting an arbitrary normal or 0, we have expressed hypertonicity of the large intestine in terms of pluses. The transverse diameter of the colon and the number of haustral markings vary in different patients and even in the same patient, at different intervals. Standards of normalcy are difficult to establish and describe. In our experience, and for the purpose of this study, the colon shown in Figure 8a may be regarded as normal. Its lumen measures about 5 centimeters in diameter and haustral markings are quite wide. Narrowing of the lumen and haustral markings was interpreted as evidence of increased colonic tone (Figs. 7a and 8b).

In the preoperative hyperthyroid patients the tone of the large intestine was definitely greater than that of the controls. After operation 13 of the hyperthyroid cases showed a decrease in tone and 2 an increase. In 5 instances the tone of the colon remained essentially unchanged, and in 4 no comparison was possible. In spite of this decrease, the colonic tone of the postoperative hyperthyroid group remained slightly greater than that of the control group. The significance of these differences is established by Methods I, III, and IV.

8. *Time colon was empty (motility of colon).* Final observations dealt with the motility of the large intestine. Following the first day's studies, daily roentgen examinations were made in order to determine in which of the succeeding 24 hour periods the evacuation of the barium from the colon was completed. Although far from ideal, this method of expressing motility was more satisfactory than our concomitant attempt to record the time and number of barium-containing bowel movements. In the preoperative hyperthyroid group, 14 of 20 cases emptied their colons of barium in less than 48 hours. In none of the controls was this true. After operation the colonic emptying time of the hyperthyroid patients had increased in 11 cases and remained the same in 5. In the remaining cases an accurate comparison could not be made. This postoperative reversion of the hyperthyroid group toward the control normal for large intestinal motility is both striking and significant (Method II).

As compared to the controls, the hyperthyroid group showed preoperatively the following differences: (1) an increased incidence of achlorhydria; (2) increased prominence of gastric rugae; (3) an increase in the rapidity with which the stomach started to empty; (4) a delay in gastric emptying (increased gastric emptying time); (5) increased small intestinal tone with an abnormal pattern; (6) increased small intestinal motility (decreased time to cecum); (7) increased large intestinal tone; (8) increased large intestinal motility.

After operation, the gastrointestinal picture presented by the hyperthyroid cases more closely resembled that of the controls. In many instances differences had entirely dis-

TABLE IV

	Gastric rugae* Means	Gastric emptying time min. Means	Small intestinal tone and pattern Means	Time to cecum min. Means
1. Age				
<36½ yrs.†	2.167	246.9	2.750+'s	55.4
>36½ yrs.	2.083	248.9	1.958+'s(S)	91.1
2. Sex				
Males	2.125	237.5	1.625+'s	94.6
Females	2.125	253.0	2.719+'s(S)	62.6
3. Pulse rate				
<103†	1.700	198.3	2.500+'s	67.1
>103	2.429(S)	283.2(S)	2.250+'s	77.6
4. Duration symptoms				
<7 mos.†	2.400	270.5	2.400+'s	89.5
>7 mos.	2.000	239.2	2.346+'s	63.7
5. Percent wt. loss				
<15½ lbs.†	2.333	247.1	2.750+'s	68.8
>15½ lbs.	1.917	248.6	1.958+'s(S)	77.7
6. B.M.R.				
<+60†	1.800	205.0	2.600+'s	74.6
>+60	2.357	278.4	2.179+'s	72.3
7. Hemoglobin				
<81†	2.545	286.4	2.727+'s	75.6
81 or more	1.769(S)	215.2	2.038+'s(S)	71.2
8. Achlorhydria				
Yes	2.000	283.1	2.500+'s	71.4
No	2.188	230.2	2.281+'s	74.2
9. Serum protein				
<6.095†	2.250	242.5	2.125+'s	66.4
>6.095	2.000	253.2	2.583+'s	80.1
10. Nausea and vomiting				
Yes	1.600	194.6	2.200+'s	70.0
No	2.263	261.8	2.395+'s	74.1
11. Appetite increase				
Yes	2.267	266.7	2.400+'s	70.5
No	1.889	216.4	2.278+'s	77.8
12. Indigestion				
Yes	2.143	279.0	2.429+'s	54.6
No	2.118	235.0	2.324+'s	80.9
13. Bowel habits				
Constipation	1.750	245.8	2.500+'s	43.8
Diarrhea	2.500	274.2	2.500+'s	79.3

*Values assigned: Normal—1; Prominent—2; Very Prominent—3.
†The median value of all hyperthyroid cases.
(S) Difference in means is significant.

appeared. Generally speaking, the changes toward normal with respect to motility were more complete than the changes in tone or pattern.

Several factors were studied for a possible relationship to the gastrointestinal variations observed in the preoperative hyperthyroid patients. Considerations governing the selection of these factors for analysis were numerous. The hyperthyroid and control groups differed somewhat in age and sex distribution. So it was necessary to investigate the possibility of a casual relationship between these two factors and the gastrointestinal differences.

Attempts were made to correlate the gastrointestinal variations with the effects of the thyrotoxicosis on other organs or systems of the body and with the basal metabolic rate and duration of the disease. Finally we tried to explain the gastrointestinal symptoms presented by our hyperthyroid patients on the basis of the underlying changes in physiology as determined by our roentgen studies. In Table IV are presented the results of our investigations with respect to prominence of gastric rugae, gastric emptying time, small intestinal tone and pattern, and time to cecum. We were not able to discover any one factor among the many studied which bore a constant relationship to all of the gastrointestinal variations studied. Only in isolated instances was there evidence of correlation. These will be discussed briefly.

Age. Age apparently had little influence on the phases of gastrointestinal activity under investigation with one possible exception. Small intestinal tone was greater and the pattern was more abnormal in the hyperthyroid subgroup below the median age. However, an age influence in this direction serves to increase rather than detract from the significance of the differences observed in small intestinal tone and pattern when the hyperthyroid patients were compared with the younger controls.

Hemoglobin level and pulse rate. The hemoglobin level apparently bore a significant relationship to prominence of gastric rugae and to small intestinal tone and pattern. The rugae were more prominent and the small intestinal tone was greater in the subgroup with hemoglobin values below the median. Pulse rate was correlated with gastric rugae and gastric emptying time. The rugae were more prominent and the stomach emptied more slowly in the subgroup with pulse rates above the median.

Sex and weight loss. Two other isolated relationships were noted. The small intestinal tone and pattern showed greater alteration in female hyperthyroid patients than in males and also in those individuals whose weight loss was above the median as compared to those below.

Achlorhydria and serum protein level. Two negative findings merit special attention. One is the lack of correlation between achlorhydria and gastric emptying time. Established teaching postulates a more rapid gastric emptying in the presence of achlorhydria. Bockus, Bank, and Willard found this true in 87 or 41.4 per cent of 210 cases of achlorhydria studied by them. Either this effect of achlorhydria was absent in our cases or the factor or factors which increase gastric emptying time in hyperthyroid patients have more than compensated for this tendency to rapid emptying.

The influence of the serum protein level upon certain phases of gastric and intestinal motility has been demonstrated both in the experimental animal and in various pathological states in humans (2, 3, 36). However, there was a complete lack of correlation between the slightly altered serum protein values and the gastrointestinal variations in our hyperthyroid patients.

Vitamin B complex deficiency. One factor which may have played an etiological rôle in the production of the gastrointestinal abnormalities observed in our hyperthyroid patients is a vitamin B complex deficiency. Cowgill has shown that the vitamin B requirement of man is greatly increased by elevations in metabolic rate, and there is much accumulated evidence (17, 21, 43) pointing to an actual deficiency in this vitamin in many cases of hyperthyroidism.

The effect of a B complex deficiency on gastric emptying and small intestinal motility has been studied roentgenologically by Heublein, Thompson, and Scully. Dogs were used as experimental animals. A B complex deficiency caused marked delay in gastric emptying similar to that observed in our hyperthyroid patients. Although the vitamin deficient dogs showed a moderate delay in small intestinal motility, the most consistent abnormality in the small intestinal pattern was that of diminished bowel caliber with hypertonic appearance. This, too, is comparable to the picture in our hyperthyroid group.

If we are justified in comparing these roentgenological observations in the experimental animal with those in our human subjects, the proposed etiological relationship between B complex deficiency and the gastrointestinal abnormalities observed in our hyperthyroid patients is supported by the similarity of these findings.

Scatter diagrams 1 to 13 were prepared in our search for interrelations between the various gastrointestinal observations themselves. No significant correlations were found either visually or by computing the measures themselves (Methods VI and VII).

Failure to establish interrelations between the various gastrointestinal abnormalities found in our hyperthyroid patients does not necessarily detract from the significance of our observations. In comparison with the controls the hyperthyroid patients as a group showed a delay in gastric emptying and an increase in small intestinal motility. It does not follow, however, that the hyperthyroid individual with the longest gastric emptying time must have the shortest time to cecum or vice versa; especially since this relationship cannot be demonstrated within the control group itself.

Neither does the lack of correlation between the gastrointestinal abnormalities and the other signs and symptoms of hyperthyroidism argue against a common etiological factor. Hyperthyroidism is a disease noted for its "dispersion phenomena" (44), that is, for the variable intensity of its effects on the different organs or systems of the body. In any given case of thyrotoxicosis one sign or symptom, or even a group of symptoms, may dominate the clinical picture and bear no relationship to the severity of the other manifestations of the disease.

SUMMARY AND CONCLUSIONS

We have studied the gastrointestinal tract in 24 hyperthyroid patients and 14 normal controls. Differences between the two groups have been noted and subjected to careful

statistical analysis in order to establish their significance. As a result of these studies we feel justified in concluding that the following gastrointestinal changes are characteristic of hyperthyroidism:

1. An increased incidence of achlorhydria.
2. Increased prominence of gastric rugae.
3. An increase in the rapidity with which the stomach starts to empty (of questionable significance).
4. A delay in gastric emptying (increased gastric emptying time).
5. Increased small intestinal tone with an abnormal pattern.
6. Increased small intestinal motility (decreased time to cecum).
7. Increased large intestinal tone.
8. Increased large intestinal motility.

APPENDIX

A. Definition of degrees of significance. Two types of differences have been encountered in the statistical study, (a) the difference between an actual finding and a hypothetical value, and (b) the difference between the actual findings in two groups. In each instance, however, the statistical problem is to test the permissibility of the hypothesis that there is no difference between the two values involved. The solution of this problem requires the determination of the probability of obtaining a difference as great or greater than the one actually occurring if chance alone had operated. The definitions of the varying degrees of significance used throughout this study are related to this probability in the following way.

Probability	Degree of significance
1. Greater than 0.05	Not significant
2. 0.05 to 0.01 exclusive	Significant
3. 0.01 or less	Highly significant
4. 0.001 or less (rarely determinable from prepared tables)	Very highly significant

B. Methodology. Various methods have been used in the statistical analysis of the data. These may be explained in brief as follows:

Method I. Determining the significance of the difference between an observed and a hypothetical ratio.

Let p be the hypothecated ratio of the expected events to the number of cases.
Let $q = 1-p$
Let n = the number of cases
The binomial, $(p+q)^n$, was then expanded and the desired probabilities were determined exactly, because the successive terms of the expansion give the probabilities that (1) $\frac{n}{n}$ (2) $\frac{n-1}{n}$ (3) $\frac{n-2}{n}$ etc., events will actually be obtained if chance alone operates.

Method II. Determining the significance of the difference between two observed percentages.

Let p_1 = the observed ratio in the preoperative group
Let p_2 = the observed ratio in the postoperative group
Let $q_1 = 1-p$
Let $q_2 = 1-p_2$
Let n_1 = number of determined cases in preoperative group
Let n_2 = number of determined cases in postoperative group

Let $p_{1+2} = \frac{n_1p_1+n_2p_2}{n_1+n_2}$

Then $SE_{p_1-p_2}$ (the standard error of p_1-p_2) $= \sqrt{p_{1+2}\, q_{1+2}\frac{n_1+n_2}{n_1n_2}}$ and the probability may be determined from prepared tables for the ratio $\frac{p_1-p_2}{S\,E\,p_1-p_2}$

(See Croxton and Cowden *Applied General Statistics*, p. 338, 339, New York: Prentice-Hall, Inc.).

Method III. Determining the significance of the difference between the means of two groups: t = test

(See R. A. Fisher's *Statistical Methods for Research Workers*, 6th ed., p. 130. London: Oliver and Boyd, 1936).

Method IV. Determining the significance of the mean difference of paired items: t-test (R. A. Fisher, op. cit., p. 126, example 19).

Method V. Determining the significance of the difference of the variability of two groups: z-test (See Croxton and Cowden, op. cit., pp. 344–348).

Method VI. Determining the significance of the difference of the Pearsonian coefficient of correlation from zero: t-test (See Croxton and Cowden, op. cit., pp. 681, 682).

Method VII. Determining the rank difference coefficient of correlation (See Croxton and Cowden, op. cit., pp. 685, 686).

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SMOOTH MUSCLE TUMORS OF THE GASTROINTESTINAL TRACT AND RETROPERITONEAL TISSUES

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IN recent years a number of very interesting benign and malignant leiomyomas of the gastrointestinal tract have been observed at the Presbyterian Hospital and in the laboratory of Surgical Pathology of Columbia University, and the striking characteristics exhibited by a few of these have stimulated a study of all neoplasms of this classification available in the hospital and laboratory records. To complete this investigation, a comprehensive analysis of the literature was undertaken and it was hoped that such a review might reveal a definite pattern for these tumors. More than 400 publications were examined and such confusion was found that reliable detailed statistics could not possibly be computed, but correlation of the substance of this material with the conclusions drawn from the series of cases at hand makes it possible to offer several basic general principles, which, it is hoped, will be of value diagnostically and therapeutically.

Seldom does this type of gastrointestinal tumor receive the benefits of more than a brief paragraph or two in the standard textbooks and this is truly incomprehensible when the mass of literature is considered. Because of this undeserved obscurity the correct preoperative diagnosis is seldom made, and the treatment instituted has not always been the most desirable one. The present study has been undertaken with the hope of clarifying our knowledge concerning these tumors.

During the 26½ year period from October, 1913 to May, 1940, 60 smooth muscle tumors of the gastrointestinal tract and retroperitoneal regions have been studied (Table I)—56 came from the Presbyterian Hospital and 4 came from other sources. Thirty of these caused clinical symptoms and all but 8 were treated by surgical removal. Four retroperitoneal tumors were subjected to biopsy only, 1 was treated with roentgenotherapy, and in 1 gastric and 2 duodenal cases patients were not operated upon because of a failure to make the diagnosis. The rest were all small intramural tumors, 7 of which were found by chance at operation (Table II), and 23 were incidental findings at autopsy[1] (Table III). This makes an incidence of 0.39 per cent of our autopsy population. Rieniets (1930) reported an incidence of 16 per cent in 200 consecutive autopsies performed at the Mayo Clinic.

Our investigation is concerned especially with those tumors which caused symptoms; a total of 30 cases (Table IV). These were distributed as follows: stomach, 8; duodenum, 2; jejunum, 1; ileum, 3; Meckel's diverticulum, 1; colon, 2; rectum, 5; retroperitoneal, 8.

After prolonged study we have tentatively concluded that 21 of them should be classified as malignant and 9 as benign. All of the smooth muscle tumors found by chance were considered benign, which gives 65 per cent benign and 35 per cent malignant in the whole group. For reasons which will presently appear, we do not feel at all confident that this division is accurate and above criticism, and we have therefore been uncertain about the question of nomenclature. Ghon and Hintz (1909) suggested that the term malignant leiomyoma be used instead of leiomyosarcoma and this is approved by Clerici Bagozzi (1934), Klopp and Crawford (1935), and Ewing (1940). As will be shown, one can never be entirely certain that any leiomyoma is necessarily benign, except the small intramural tumors which are chance findings at autopsy or operation. Any of the tumors large enough to cause clinical symptoms *may* kill by infiltrative growth or occasionally by metastasis, although as a matter of record very few of

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[1]We are indebted to Dr. J. W. Jobling, professor of pathology of Columbia University, for permission to include these and 4 other clinical cases which came to autopsy.

TABLE I.—DISTRIBUTION AND CLASSIFICATION OF 60 SMOOTH MUSCLE TUMORS

Site	Cases	Clinical	Incidental at operation	Incidental at autopsy	Malignant	Metastases	Recurrence
Stomach	33	8	5	20	5	2	0
Duodenum	3	2	0	1	1	1	0
Jejunum	1	1	0	0	1	0	0
Ileum	5	3	0	2	2	0	1
Meckel's diverticulum	1	1	0	0	1	0	0
Colon (left)	3	2	1	0	1	0	0
Rectum	5	5	0	0	4	0	1
Retroperitoneal	9	8	1	0	6	3	1
Total	60	30	7	23	21	6*	3**

*29% of 21 malignant leiomyomas, 19% of 30 clinical leiomyomas.
**14.5% of 21 malignant leiomyomas, 9.5% of 30 clinical leiomyomas.

TABLE II.—7 INCIDENTAL LEIOMYOMAS FOUND AT OPERATION

Case	Sex Age	Operation	Site	Size
31	F 63	Colostomy and perineal proctectomy for carcinoma of rectum. Excision of leiomyomas	Stomach and right ovary	Each—2 cm.
32	M 54	Subtotal gastric resection for gastric ulcer	Stomach	3 by 2 mm.
33	F 61	Subtotal gastric resection for gastric ulcer	Stomach	7 mm.
34	M 66	Subtotal gastric resection for carcinoma	Stomach	7 by 3 mm.
35	M 42	Excision of hypernephroma of left kidney. Excision of leiomyoma	Stomach	2 by 1.5 by 1.5 cm.
36	M 57	Abdominoperineal resection for carcinoma of rectum	Sigmoid colon	1.5 by 1.5 cm.
37	M 65	Appendectomy and excision of leiomyoma	Omentum	4 mm.

them do so. There is no basic objection to the use of leiomyosarcoma instead of malignant leiomyoma, for in both instances the term connotes a malignant smooth muscle tumor. But in the minds of many the word "sarcoma" suggests a high degree of malignancy and, as we shall show, the malignant smooth muscle tumors as a group do not justify this reputation. For this reason, we favor the use of "malignant leiomyoma" for those tumors which exhibit histological or clinical evidences of malignancy.

The *etiological factors* involved remain entirely speculative and range from theories concerned with congenital anlage (Cohnheim-Ribbert) to suggestions that these tumors result from inflammatory stimulation of smooth muscle tissue (Virchow). It is not possible, therefore, to state definitely anything more than the fact that these tumors originate in the muscularis of the gastrointestinal tract. Rarely, the site of origin is the muscularis mucosae (Fig. 26), and it is further conceivable that the vascular musculature may give rise to a leiomyoma.

There is no demonstrable difference in *incidence* based on sex, race, or geography. In general, 60 per cent occur between 40 and 60 years, while 20 per cent are under 40 and 20 per cent over 60. The average age approximates 47 and the youngest patient was a 2 year old African male child (Kroeber, 1934), while the oldest was an 81 year old male (Ghon and Hintz, 1909). By far the commonest reported site of occurrence is the stomach, with a total of 629 cases (61.5 per cent). Then, in order of frequency, are the following: small intestine, including appendix and Meckel's diverticulum—197 cases, 19 per cent; rectum—69 cases, 7 per cent; duodenum—51 cases, 5 per cent; retroperitoneal tissue, including omentum and mesenteries—43 cases, 4.5 per cent; and colon—29 cases, 3 per cent; a total of 1,018 cases. It is safe to assume that many more have been unreported, unrecognized, or incorrectly diagnosed.

In general, 60 per cent of the gastric tumors occur in the pyloric region, 25 per cent in the pars media, and 15 per cent in the cardia. They exhibit a predilection for the curvatures, with the lesser more frequent in the ratio of 3 to 2, and twice as many are found on the posterior as on the anterior surface.

In the small intestine, 80 per cent occur with equal frequency in the ileum and jejunum, while 20 per cent are found in the duodenum. Rarely, the appendix or a Meckel's diverticulum is the site of origin.

In the large bowel, 83 per cent arise in the rectum and 17 per cent in the colon. Of the latter, almost 50 per cent occur in the cecum.

PATHOLOGY

In the gastrointestinal tract both benign and malignant tumors are firm, occasionally indurated, well defined, rounded, or lobulated

TABLE III.—23 INCIDENTAL LEIOMYOMAS FOUND AT AUTOPSY*

Case	Autopsy	Sex Age	Site	Size
1	8325	M 66	Stomach	4 mm.
2	8477	M 75	Stomach (2)	3.5 by 3.25 cm. & 2 mm.
3	9160	M 53	Stomach (2)	Larger—6 mm.
4	9565	M 65	Stomach	4 by 3 mm.
5	9846	F 58	Stomach	7 mm.
6	9930	M 93	Stomach	3 mm.
7	9940	M 60	Stomach	6 mm.
8	9988	M 58	Stomach	6 by 4 mm.
9	10244	F 57	Stomach	3 mm.
10	10931	F 57	Stomach (2)	Each—7 mm.
11	11453	F 69	Stomach and left broad ligament	5 mm. and 6 mm., respectively
12	11667	M 54	Stomach	1 by 0.5 cm.
13	11987	M 63	Stomach (2)	Largest—5 mm.
14	11990	F 70	Stomach	1.5 cm.
15	12252	F 61	Stomach	5 mm.
16	12386	F 65	Stomach	4 by 1 by 1 cm.
17	12492	F 78	Stomach	5 mm.
18	12523	M 44	Stomach	2 mm.
19	12732	M 65	Stomach	4 mm.
20	12948	M 49	Stomach	6 by 4 by 4 mm.
21	8289	M 56	Ileum	5 mm.
22	10703	M 70	Ileum	1 cm.
23**	12321	M 70	Duodenum and peripancreatic	Duodenal—5 cm. Peripancreatic 0.5—1 cm.

*Found in a total of 5,869 autopsies. Incidence—0.39 per cent.
**A most unique case. It is remarkable that a leiomyoma of considerable size in the duodenum, such as this, remained entirely silent during life.

TABLE IV.—RESULTS IN 30 CLINICAL SMOOTH MUSCLE TUMORS

Site	Cases	Living with no disease	Died of disease	Operative death	Died of intercurrent disease	Living with disease
Stomach	8	4	3	1	0	0
Duodenum	2	0	2	0	0	0
Jejunum	1	1	0	0	0	0
Ileum	3	1	1	1	0	0
Meckel's diverticulum	1	1	0	0	0	0
Colon (left)	2	2	0	0	0	0
Rectum*	5	2	0	1	1	0
Retroperitoneal	8	1	3	2	0	2
Total	30	12	9	5	1	2

*No follow-up available in one case.

masses, usually sessile, but often pedunculated, varying in size from less than 5 millimeters up to 20 to 30 centimeters in diameter and weighing as much as 6500 grams. Multiple growths are quite infrequent. They are sharply circumscribed, but microscopically a definite capsule is seldom seen. The cut surface presents a grayish-pink, whorled or "watered-silk" appearance (Figs. 4 and 21). But, attributable chiefly to the relative avascularity of the tumor, regressive and inflammatory changes, such as fibrosis, necrosis, cavitation, hemorrhage, abscess formation, calcification, and cyst formation commonly supervene, so that the gross picture is usually quite variable (Figs. 2, 11, and 19).

Starting in the muscle coats, growth occurs toward or away from the lumen of the bowel, or in both directions, and Virchow, in 1863, first described leiomyomas as *inneren* (submucosal) or *ausseren* (subserosal). The preferred designation names the region involved, modified by the prefix endo- or exo-, as the case may be (e.g., endoenteric leiomyoma of ileum). In addition, the term "hour-glass" indicates the less common combined form and "intramural" describes the type which remains small, benign, and is always an incidental finding at operation or autopsy. These intramural leiomyomas are usually less than 1 centimeter in diameter and, although circumscribed, are practically never encapsulated.

With the exception of the tumors of the rectum, the overlying mucosa covering the submucosal masses commonly becomes ulcerated. Hemorrhage within the tumor frequently oc-

curs and, when associated with ulceration, the blood is discharged into the gastrointestinal tract (Figs. 4 and 8). Uncommonly, a neoplasm becomes necrotic or infected and perforates into the peritoneal cavity, with a resultant generalized peritonitis (Cases 2, 10).

The retroperitoneal tumors usually grow to the largest dimensions, are commonly less well defined and undergo similar degenerative changes. They almost always involve surrounding vital structures by direct extension and may even erode portions of the vertebral column (Case 29).

The histology of these tumors is much like that of smooth muscle tumors in other parts of the body with a few interesting variations. The smooth muscle cells with their myofibrils and an accompanying framework of connective tissue are arranged in bundles which tend to interlace (Figs. 6, 12, 15, 23). The spindle-shaped cells resemble smooth muscle cells to a greater or less degree, depending apparently upon rapidity of growth and regularity of mitotic division, but also upon phenomena of degeneration, so that the formation of bizarre or monster cells may be an indication either of atypical growth or degeneration (Figs. 3 and 20). A rather striking feature is the tendency of the nuclei to be aligned in palisade formation (Figs. 6, 9, 12, 15). It was observed in all but 6 of the tumors in our series. Seemingly it is much more common in this group of leiomyomas than in those found in other parts of the body. This fact, together with the tendency for the gastrointestinal leiomyomas to undergo patchy necrosis simulating the type B tissue of the neurilemmoma (Fig. 24), has led a number of writers (Gosset, et al., 1924; Abadie and Argaud, 1928; Jeanneney, 1933; Tierney, 1934; Ransom and Kay, 1940) to confuse smooth muscle tumors with nerve sheath tumors. One of the present writers was similarly misled and reported 3 gastric tumors as neurilemmomas (Stout, 1935; Cases 6, 17, and 30). These are now reclassified and included in the present group as Cases 35, 31, and 6, respectively.

This group of smooth muscle tumors differs from those in the uterus and subcutaneous tissues by the fact that they are not encapsulated, but their cells and fibers interdigitate with uninvolved tissue at the periphery (Figs. 6 and 12). This makes it appear as if they were infiltrating growths, and no doubt has influenced some writers to classify them as malignant tumors. This is an unjustifiable criterion, for it occurs in practically all of the small intramural tumors found by chance at autopsy or operation (Fig. 25). This lack of encapsulation is of aid in differentiating the leiomyoma from the neurilemmoma, for the latter is always an encapsulated tumor.

One might suppose that the presence or relative absence of myofibrils could be used as a standard of relative differentiation, whereby it would be possible to judge degrees of malignancy. Unfortunately, this is not a reliable criterion. There are some tumors in this series, such as in Case 4, in which myofibrils could be found not at all, or only with the greatest difficulty and yet which have given no biological evidences of malignancy. On the other hand, Case 24 was always well supplied with myofibrils and yet is certainly malignant, since it metastasized. The demonstration of myofibrils is convincing proof of the nature of these tumors. We would emphasize the facts that good fixation and differential staining are essential to the accomplishment of this. Without them histological diagnosis is a matter of guesswork.

As in the uterine leiomyomas the size and shape of the cells is not necessarily a criterion of relative malignancy. A malignant leiomyoma may be composed of cells which show few differences from normal smooth muscle cells (Case 4, Fig. 6; Case 5, Fig. 9; Case 19, Fig. 23), while on the other hand some tumors in which bizarre cells are formed may not be clinically malignant (Case 15, Fig. 20). It is quite possible that in such cases the formation of bizarre cells is an indication of degeneration rather than hyperactivity.

The relative number of mitoses is an infallible indication of growth activity and relatively important as a criterion of malignancy. If two or more mitoses per high power field are present, one can feel fairly secure in predicting malignancy. But the converse of this is not true, for some clinically malignant tumors have shown relatively few mitoses (Cases 18 and 24).

The literature indicates that the benign tumor is eight times as frequent as the malignant in the stomach, while in the rest of the intestinal tract the ratio approaches 4 to 1. In the present series the ratio, when all cases are considered, is approximately 2 to 1, but if the 30 chance findings are excluded, the malignant leiomyoma occurred twice as often as the benign. Cases in which a histologically benign leiomyoma is associated with metastases have been reported (Hunt, 1923; Demel, 1926; Melnick, 1932), and in general the incidence of metastases is approximately 30 per cent of the malignant cases (Table I). Metastasis occurs most commonly to the liver, while rarely the lung and peritoneum are involved. Cellina (1931); Brink and Laing (1933); Pack and McNeer (1935); and Gottlieb and Reitman (1939) have reported metastases to the regional lymph nodes. We cannot comment upon this finding, since we have not personally studied these cases. Metastasis of malignant smooth muscle tumors primary in any part of the body to lymph nodes has never been observed by us. Generalized metastases involving distant organs have been reported in only two instances (Pack and McNeer, 1935; Ghon and Hintz, 1909).

Curiously, there are no reports of metastasis from a retroperitoneal smooth muscle tumor, but in the present series 3 of the 8 primary cases were associated with this complication. There is only 1 instance of metastasis from a rectal leiomyoma (Wright and Hall, 1932), but the incidence of recurrence in both regions is at least 25 per cent. The most plausible explanation for this seems to be that in these two regions a complete peritoneal barrier is lacking and even with apparently wide local excision of the tumor one or more occult nodules may be left behind.

SYMPTOMATOLOGY

The symptomatology by which these tumors manifest themselves is quite varied in severity and duration, and no typical or pathognomonic signs are available. In the interests of clarity, the clinical considerations are presented according to the regions involved.

Stomach. Although the endogastric and exogastric leiomyomas are of approximately equal incidence, the degeneration and ulceration which almost always complicate the endogastric tumors account for the high frequency of hemorrhage. This occurs in over 50 per cent of the cases and is manifested by hematemesis, melena, and secondary anemia. Occasionally there may be bleeding in a case with an apparently intact mucosa and in some instances massive hemorrhage occurs in an exogastric tumor, being discharged into the gastric lumen through one or more sinus tracts. Often this is the only indicative sign and the attacks of hematemesis or melena may seem innocuous, being separated by weeks or even years of uneventful good health. However, the attacks ultimately increase in magnitude and frequency and the seriousness of the condition becomes apparent. Rarely, there is sudden onset of continuous hemorrhage which terminates fatally in a few days. This is the result of erosion of a large gastric vessel and such a catastrophe is strikingly represented in this series by Case 8 (Fig. 16).

Pseudo-ulcer symptoms consisting chiefly of epigastric pain and burning, nausea, vomiting, and anorexia, usually unrelated to meals, occur in 30 per cent and evidence of pyloric obstruction is of equal frequency. Willenbacher (1928) reported a case in which an apple-sized pyloric leiomyoma caused obstruction by intermittent ball-valve action and Barnett (1925) cited an instance of gastroduodenal intussusception as a result of a pedunculated leiomyoma arising in the cardia.

A palpable abdominal mass appears in 20 per cent and may be the only clinical finding, as in Case 7 (Fig. 14), while in 10 per cent there are vague complaints of weakness, fatigue, malaise, headache, and dizziness without special reference to the gastrointestinal tract. In the presence of coexistent disease in the stomach or elsewhere, the smooth muscle tumor may, and usually does, remain entirely silent.

Except in the rare highly malignant leiomyomas which run a fulminating course (Case 1, Figs. 2 and 3), cachexia, prostration, and marked weight loss are inconsequential factors and the latter seldom exceeds 10 to 15 pounds.

The exceptional case in which an exogastric tumor perforates into the peritoneal cavity

(Wells, 1924; Baumgartner, 1939; Case 2), is evidenced by pain and fever of variable duration, culminating in the sudden onset of signs of an acute abdomen.

There are no characteristic laboratory data associated with the neoplasm in any region.

Roentgenologic examination is a decided aid to diagnosis when properly applied and evaluated, but the typical configuration is common to all benign tumors and the correct diagnosis, when made, is based essentially on probabilities, since the leiomyoma is by far the most common of the benign tumors of the stomach. The following principal features, emphasized by Moore (1927) are worthy of repetition:

(a) In the endogastric tumors we find: (1) A central or marginal filling defect, usually rounded and smooth, occasionally exhibiting a crater shadow in the dome. Manual manipulation, in order to approximate the gastric walls, is essential, especially for small tumors. Sometimes a pedicle, if present, may thus be outlined. (2) There is no contraction or spasm of the stomach. (3) Peristalsis is usually uninterrupted and the gastric wall remains pliant. (4) Rugae are not obliterated as in cancer, or thrown into convergent folds, as in ulcer. (5) Multiple growths are strongly indicative of benignity.

(b) In the exogastric tumors we find the following: Exogastric tumors manifest themselves by pressure or traction, thus producing a deformity which is likely to be misinterpreted as an ulcer or cancer. Negative roentgenograms do not exclude the possibility of a tumor.

It is noteworthy that in the series presented, a correct diagnosis of hour-glass gastric leiomyoma was made in one instance by Dr. Robert P. Ball (Case 7, Fig. 13), while Dr. Ross Golden correctly identified a case of endogastric malignant leiomyoma (Case 5, Fig. 7).

Duodenum. Tumors arising in this region are associated most frequently with symptoms simulating duodenal ulcer, and hemorrhage is the most significant sign. The exoduodenal are three times as common as the endoduodenal leiomyomas and evidence of obstruction is exceptional, in sharp contrast to the rather high incidence of this complication in the rest of the small intestine.

The pars descendens is the site of origin in at least 50 per cent, but jaundice, as a result of obstruction of the common duct or ampulla of Vater, has apparently never been reported. In some cases, the tumor is responsible for constipation or diarrhea, or both, by compressing the overlying ascending or transverse colon and often it partially occludes the inferior vena cava or superior mesenteric artery, and death due to thrombosis or pulmonary embolism is of a remarkably high incidence (Case 9, also reported by Andersen and Doob in 1933; Brdiczka, 1931; Foshee and McBride, 1939; von Salis, 1920; Seymour and Gould, 1936).

A palpable tumor is present in 25 per cent of the cases and perforation of a degenerated leiomyoma into the peritoneal cavity (Case 10) is somewhat more frequent than with the gastric cases.

Roentgenologically, these tumors often manifest themselves as a deformity of the bulb or a filling defect, in common with other tumors in this region, and R. Golden (1928) suggested that these could be differentiated from gastric tumors by absence of a 6 hour residue.

Jejunum and ileum. In this region, hemorrhage, which usually cannot be localized, is again the most frequent finding. It may be slight or result fatally (Smith, 1937), but seldom is the small intestine suspected as the site of origin until a mass appears or there are symptoms of obstruction. The latter usually occurs late, but is precipitate and, although the exoenteric tumor is four times as common as the endoenteric, either type may be responsible for the intussusception, torsion, or angulation which produces the obstruction. Intussusception, in particular, is found in 30 per cent of the cases, accompanied by the usual signs.

Partial, slowly developing, increasingly severe obstruction accompanied by constipation, diarrhea, twinge-like local or generalized abdominal pain or cramps, tenderness, and occasional nausea and vomiting, is most often the result of gradual encroachment on the lumen by an endoenteric tumor. This type seldom attains the size of the exoenteric, but a palpable, freely movable mass is found in approximately one-half of all cases.

Degeneration of the tumor occurs here as often as elsewhere and is occasionally also responsible for generalized peritonitis as a result of perforation into the abdominal cavity (Feyrter, 1928; Kiefer, 1933; Goldberg, 1939; Lewis, 1939).

A Meckel's diverticulum has been the site of origin of a smooth muscle tumor in 8 reported instances and the associated symptoms are undifferentiated from those caused by the tumor elsewhere in the small intestine. Hoepfner (1912) reported a leiomyoma of a Meckel's diverticulum causing intussusception in a 9 year old boy and attempted to explain the mechanism involved. In the present series a ninth case (Case 15, Figs. 19 and 20) is added to those previously reported.

In the appendix, the symptoms most often resemble those due to acute appendicitis. The tip is the site of origin in 50 per cent and the largest tumor was 9.6 centimeters in diameter (Rosi, 1897). Only 15 cases have been reported; 14 tabulated by Koontz (1929), and the last described by Charache (1934).

Roentgenological studies are of limited value so far as these small intestinal tumors are concerned. They reveal intestinal obstruction, if present, but in no case has the tumor itself been outlined.

Colon. It has been indicated in the past by many observers that, in general, tumors of the left-sided colon usually produce obstruction, while on the right side, especially in the cecum, obstruction is rare. Smooth muscle tumors of the colon follow this rule and, since approximately 50 per cent are found in the cecum, obstructive signs are exceptional. Some of these are symptomless, while others present only a palpable mass, but in 2 cases (Jones, 1935; Trygstad, 1932), intussusception with complete obstruction occurred as a result of a cecal tumor. The less frequent left-sided leiomyomas are usually associated with signs of partial obstruction, whether the neoplasm is exocolonic or endocolonic (Case 17, Fig. 21).

The overlying mucosa is apparently less often ulcerated in this region than in the previously mentioned sites and degeneration and bleeding occur less frequently. A palpable freely movable mass appears in 40 per cent, and a barium enema ordinarily will reveal a partial obstruction, if present.

Rectum. Almost all of the smooth muscle tumors of the rectum are endorectal, within easy reach of an examining finger, although extension anteriorly or posteriorly occasionally occurs. They are seldom larger than 5 to 6 centimeters in diameter, and the rectal mucosa is usually intact. Accordingly, bleeding is rare, while partial obstruction with a narrowed stool, constipation, tenesmus, difficult and painful defecation, diarrhea of glairy mucoid material, fullness, and sensation of a mass, in varying combinations, are habitually found. There may be marked rectal spasm and pain, often radiating to the thighs or back and when the tumor grows anteriorly, symptoms of urinary obstruction are prominent. In some instances, the tumor is pedunculated and may prolapse during defecation (Case 21). Heurtaux (1856) and Hunt (1921) recorded a number of these and Longuet (1898) described 2 cases in which the pedunculated tumor was expelled spontaneously with no apparent complications.

Retroperitoneum. It is entirely impossible to decide before operation that a particular retroperitoneal tumor is of smooth muscle origin. In common with all other tumors in this region, it usually attains marked bulk, often dissects the overlying mesenteries, and the associated symptomatology is always attributable to the mechanical effects of the mass. Pressure on nerves or plexuses results in various paresthesias or backache, radiating customarily to the thighs and legs. Edema of the lower extremities and occasional ascites are associated with venous embarrassment, while pressure on the intestinal tract may cause partial or complete obstruction, and involvement of the urinary system is responsible for frequency and urgency or obstruction with infection. Although it is probably more common than indicated, in only 1 other instance besides Case 29 was erosion of the lumbosacral vertebrae reported (Magoun, 1919).

By their very nature, it is clear that, except for the rare small omental leiomyomas, all these tumors are eventually palpable as indurated, fixed masses. It is necessary, however, carefully to exclude the possibility of

tumors or cysts of the spleen, kidneys, pancreas, rectum, or pelvic organs.

TREATMENT

Morgagni, in 1762, was apparently the first observer to describe a probable smooth muscle tumor; a gastric case, but it was not until 1890 that an attempt was made to remove such a mass surgically. The operation, by Kuntze, ended fatally, but 5 years later von Erlach successfully resected a 5400 gram gastric leiomyoma in a 36 year old female. To the present time this has remained the only available form of therapy, since neither roentgen therapy nor radium implantation have any appreciable effect upon the tumor.

Gastric and intestinal leiomyomas (with the exception of those originating in the duodenum) are most amenable to excision or resection, and the operative mortality varies directly with the experience of the surgeon and the presence or absence of complications. The choice of procedure is limited to local excision through gastrotomy or partial resection followed by anastomosis, but in rare instances the tumor will prove technically inoperable. The presence of metastases, unless widespread, is no contraindication to surgery, but in such a case the primary tumor must be resected as widely as possible. In most cases no metastases are present and an attempt at deciding the question of malignancy should be made by frozen section. Admittedly, this is very difficult, but if malignant characteristics can be readily demonstrated or if reasonable doubt as to benignancy exists, a partial resection should be accomplished. If the tumor appears benign, and local excision is decided upon, a generous ring of stomach or bowel wall beyond the apparent limits of the tumor should be excised with it, since these tumors are almost never truly encapsulated. Exception must be taken to the recent inference by Lahey and Colcock (1940) that, generally, radical subtotal gastrectomy is indicated in gastric cases. If the tumor is carefully and properly evaluated, conservative removal will be adequate and least disturbing to the patient's physiological economy in the majority of instances.

Where the duodenum is the site of origin, the usual involvement of adjacent vital structures seriously complicates the surgical problem, and in some instances the surgeon may be loath to attempt removal. However, if at all feasible, a partial resection, modified as necessitated by individual characteristics, remains the patient's only hope. Fortunately, most of these tumors arise in the readily accessible pars descendens.

Rectal leiomyomas have been treated in the past most often by enucleation or, if pedunculated, by excision through the pedicle. Hunt (1921) summarized a number of previous cases, in which it appeared that enucleation or simple excision was entirely adequate, but more recently, critical observers such as Rankin and Larson (1932) and Bargen and Dixon (1934) have found that recurrence followed excision in an uncomfortably large percentage and, because of this, increasingly radical removal was necessary.

With the exception of the pedunculated tumors, the possibility of recurrence is not governed by the benignancy or malignancy of the histological picture, and it has been pointed out that occult nodules may remain even after extensive excision. Therefore, in view of the fact that it is impossible to decide definitely in advance whether or not the tumor will reappear, it is clear that radical surgery is indicated and all leiomyomas of the rectum, except for the occasional pedicled case, must be treated by abdominoperineal resection or its modification, permanent colostomy, followed by perineal proctectomy. If recurrence does eventuate, it is most likely to appear in the operative site (Case 18), and may be readily dealt with by simple excision without subjecting the patient to repeated serious surgery.

The exceptional pedunculated leiomyoma can be excised locally through its pedicle, since the possibility of recurrence in such a case appears to be remote.

Retroperitoneal tumors in general are frequently inoperable and, as Phillips (1934) has indicated, the immediate mortality in those cases in which removal is attempted is beyond 40 per cent. Often segments of small and large intestines must be removed with the mass, because of interference with blood supply and, if a particular tumor can be excised, the most radical excision possible is indicated. If com-

Fig. 1. Case 1. Roentgenogram of malignant leiomyoma of stomach. The tumor has caused an irregular filling defect along the greater curvature near the cardiac end. Barium has filled the excavation shown in Figure 2.

plete extirpation cannot be achieved, it is advantageous and advisable to remove as much of the tumor as possible by morcellation. Although this is only temporarily effective, it will usually make the patient more comfortable for an indeterminate period than if the entire tumor is left *in situ*. Case 30 in the present series is the only instance on record in which a retroperitoneal smooth muscle tumor, untreated, did not continue to grow and terminate fatally. Amazingly enough, in this particular case, the tumor is actually smaller at present (7½ years following biopsy) and entirely symptomless.

PROGNOSIS

The literature does not present a conclusive foundation on which prognosis may be based, since in only a few instances is an adequate follow-up available and often the diagnosis of malignancy is not clearly established. In general, however, it may be stated that proper surgical treatment of the benign smooth muscle tumor will result in a cure, unless the tumor is rectal or retroperitoneal. In the latter instances, and occasionally with a duodenal leiomyoma, the probability of total cure is

Fig. 2. Case 1. Malignant leiomyoma of stomach (12 by 10 by 6 cm.). The tumor lies in the posterior wall near the greater curvature with the pylorus at the left. There is a deep excavated ulcer which penetrates through the mucosa into the tumor.

rather remote, for reasons here indicated, and the prognosis must be extremely guarded.

The malignant leiomyoma is usually of low grade malignancy and if adequately treated, even in the presence of metastases, the patient may enjoy many years of uneventful health. Demel (1926) told of a 42 year old female patient in whom he found a 12 by 11 centimeter metastatic hepatic nodule of smooth muscle tissue. There was apparently no primary site and the metastatic nodule was excised. It was not until 2 years later, at autopsy, that the original tumor in the jejunum was seen, and there were many additional large liver metastases.

However, where the histological picture indicates a poorly differentiated tumor, with many mitoses and bizarre forms, the duration of life, even with radical removal, appears to be little more than a year or two following the onset of symptoms. Fortunately such cases are uncommon. With this exception, it appears that the benign and malignant types are often similar in action and therefore no sharp clinical distinction has been made between the two.

In the present series, several of the cases have approached a 10 year follow-up, and Judd and Hoerner (1936) reported a stomach case alive 22 years after operation, but more cases must be followed for longer periods before definite conclusions can be drawn. It can be stated, however, that most of these tumors

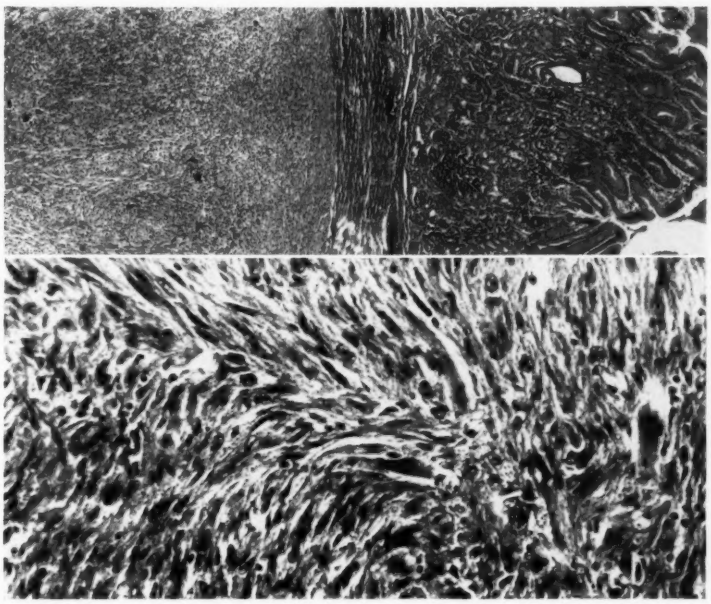

Fig. 3. Case 1. Malignant leiomyoma of stomach. Above, Relationship of tumor to the submucosa and mucosa. Below, The tumor is composed of interlaced bundles of spindle cells showing mitoses and monster forms.

appear to be less malignant than the majority of cancers, and if recognized early enough and treated properly they usually offer at least a fair prognosis.

CASE REPORTS[1]

Stomach

CASE 1. S. P. 35506. Unit Hist. No. 67090. P. L., a 43 year old white Italian male was first admitted to the Presbyterian Hospital, October 26, 1926, with a 5 months' history of indigestion, feeling of heaviness, constipation, headache, marked nausea, and lower abdominal cramps, relieved by soda. Jaundice at onset, then chills and afternoon fever intermittently. Vomiting on two occasions: once foul, coffee-ground material. No melena. There was marked weakness, dyspnea and a loss of 20 pounds in weight. Symptoms were aggravated during previous 3 weeks.

Examination revealed a poorly nourished male showing evidence of marked weight loss, dyspnea and pallor. Skin icteric. Epigastric tenderness was well defined, but no masses were palpable. Stool guaiac, ++++. Barium series showed a broad, irregular filling defect in the greater curvature of the stomach about 2.5 centimeters below the upper surface of the fundus (Fig. 1). Peristalsis did not pass over the greater curvature. A diagnosis of carcinoma of the stomach was made and surgery was advised, but, with symptomatic improvement, the patient rejected this advice and left the hospital November 13, 1926.

He returned at the end of 3 months quite improved, and on February 14, 1927, a sleeve resection of the gastric tumor was performed by Dr. Fordyce B. St. John. The tumor was firm, lobulated, and chiefly endogastric, lying in the posterior wall of the pars media near the greater curvature. There were several large subserosal projections, and the overlying vessels were quite prominent and markedly distended. The mass measured 12 by 10 by 6 centimeters and there was a crater-like excavation in its midportion measuring 5 by 4 by 2 centimeters. There was no evidence of metastasis (Fig. 2).

Microscopically, the tumor was sharply circumscribed, lying between the submucosa and muscularis. It was composed of freely interlaced bundles of large, elongated cells, with hyperchromatic nuclei. Mitoses averaged 1 in every 2 high power fields and there were scattered bizarre forms as well as occasional multinucleated cells (Fig. 3). Preparations adequate for the demonstration of myofibrils were not available.

Diagnosis: Malignant leiomyoma of stomach.

The immediate postoperative course was satisfactory, and the patient was discharged March 24, 1927,

[1] The illustrative cases are presented in detail.

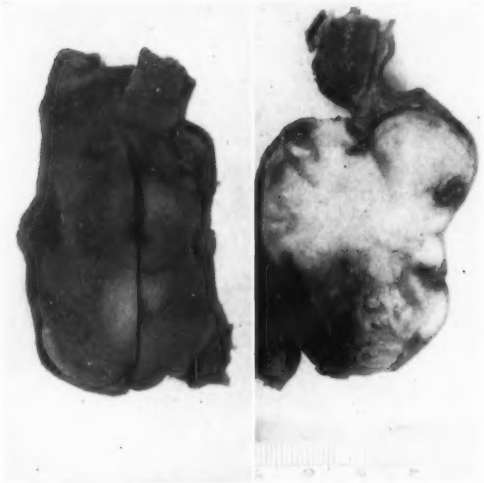

Fig. 4. Case 4. Malignant leiomyoma of stomach (6.5 by 4.5 by 4 cm.). The tumor is covered by thin mucosa. In the line of incision are 3 small ulcerations.

The cut surface presents a glistening "watered-silk" appearance with one large area of hemorrhage. This communicated with the gastric lumen through one of the ulcerations.

greatly improved. He gained 17 pounds during the first month, but soon began to lose ground rapidly and was again admitted November 19, 1927, complaining of loss of strength, dyspnea, pain in incisional line, and loss of 10 pounds in weight. A 2 centimeter nodule was found in the midportion of the incisional scar and a roentgenogram revealed marked pulmonary metastases. He was given symptomatic care, his condition was evidently hopeless, and he was discharged November 27, 1927. He went rapidly downhill, developing a severe cough with orthopnea, and expired at home January 4, 1928, 20 months after onset of symptoms and 11 months following resection of the tumor. No autopsy could be obtained.

Final diagnosis: Malignant leiomyoma of stomach with metastases to lungs and probable implantation in abdominal scar.

Case 2. S. P. 56225. Unit Hist. No. 433406. B. H., a 57 year old white American male was admitted to the Presbyterian Hospital, October 20, 1934, with a 2 months' history of a right upper quadrant abdominal mass, weakness, anemia, constipation, and elevated temperature. Seven months before admission, there had been a sudden onset of severe right lower quadrant abdominal pain, and a large tender mass in this area. He was operated on in Newark, New Jersey, and an appendiceal abscess containing the remnants of a perforated appendix was found. The upper abdominal mass developed soon after recovery.

Examination revealed marked anemia, a well defined upper abdominal mass, and an enlarged, nodular liver. A barium series showed no definite disease within the gastrointestinal tract.

On December 15, 1934, an exploratory laparotomy was performed by Dr. Allen O. Whipple. The mass itself could not be resected, and there were two metastatic nodules in the liver. The tumor was biopsied. Roentgenotherapy was instituted after operation, but proved of no value. The patient went downhill rapidly, developed terminal signs of a diffuse peritonitis, and expired on January 20, 1935, 5 months after onset of symptoms.

At autopsy (No. 11724), the tumor was found in the lower half of the stomach. It was a degenerated, friable, exogastric mass measuring 20 by 12 centimeters. An ulceration in the overlying mucosa led directly into a central abscess cavity which had further ruptured into the peritoneal cavity, resulting in a generalized peritonitis. Two large, firm, whitish metastatic nodules were in the right lobe of the enlarged liver.

Microscopically, the biopsy consisted of tumor tissue invading the gastric muscularis and projecting slightly into the lumen of the stomach as an ulcerated mass. It was made up of parallel, interlaced bands of smooth muscle cells varying considerably in size and shape. The nuclei were often hyperchromatic and a number of multinucleated forms were seen. Myofibrils could not be clearly demonstrated. Mitotic figures averaged 1 in every high power field and occasionally assumed bizarre forms. There was a considerable fibrous stroma containing a moderate number of small blood vessels. Autopsy sections were similar.

Diagnosis: Malignant leiomyoma of stomach with metastases to liver.

Case 3. S. P. 72684: 72954. Unit Hist. No. 565708. Autopsy No. 13,237. J. B., a 43 year old obese colored male was admitted to the medical service of the Presbyterian Hospital from the Vanderbilt Clinic, November 19, 1939, for a thorough gastrointestinal work-up. He had complained for a year of gas pains, unrelated to meals, and flatulence. He had been treated in the clinic for mild secondary anemia. In the last 3 months he had developed a tender mass in the left upper quadrant and had lost a total of 35 pounds during the year.

Physical examination revealed a firm, movable, somewhat tender, nodular abdominal mass on the left side, extending from under the costal margin to the iliac crest. Temperature, pulse, and erythrocyte sedimentation rate were moderately elevated and there was a secondary anemia. Stool guaiac, ++++.

Five days after admission, a roentgenogram revealed a large mass behind the stomach displacing it forward and causing a pressure defect along the greater curvature posteriorly. It appeared to represent an intra-abdominal tumor secondarily invading the stomach and on November 29, 1939, a biopsy specimen was removed from it.

Fig. 5. Case 4. Malignant leiomyoma of stomach. One of the ulcerations in the tumor.

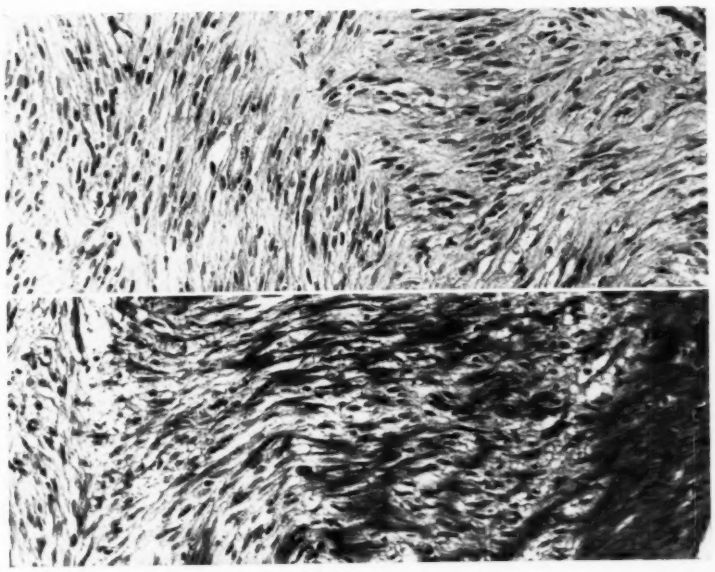

Fig. 6. Case 4. Malignant leiomyoma of stomach. The tumor is composed of interlaced bundles of spindle cells. Palisaded nuclei are shown in the area above and interdigitation of tumor with the muscle coat below.

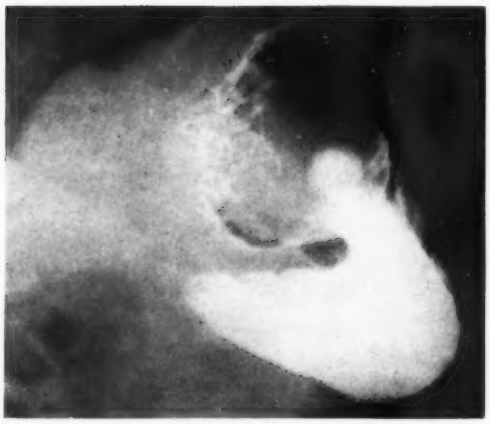

Fig. 7. Case 5. Roentgenogram (recumbent, oblique view) of malignant leiomyoma of stomach (diagnosis made before operation). The tumor makes a smooth, rounded filling defect, and barium fills an ulcer-crater in the dome.

The biopsy was composed of elongated, intertwined and whorled smooth muscle cells, with plump nuclei occasionally arranged in atypical palisades. There was some irregularity in cellular size and shape, but mitoses were scarce. Myofibrils could not be demonstrated. The connective tissue stroma was scanty, poorly vascularized, and there were scattered areas of necrosis.

Diagnosis: Malignant leiomyoma of stomach.

Following the biopsy examination, the advisability of further surgery was the subject of much discussion, but it appeared that intragastric hemorrhage was becoming more severe, the patient's condition was increasingly critical, and the prognosis apparently hopeless. It was therefore decided that a desperate chance had to be taken and on December 29, 1939, Dr. Hugh Auchincloss attempted to remove the tumor. It measured 20 by 13 by 7.5 centimeters and weighed 985 grams. It was almost entirely necrotic and arose in the posterior aspect of the stomach along the greater curvature communicating with its lumen through a broad sinus tract. It grew exogastrically, involving the pancreas, transverse mesocolon and partially surrounded the aorta in this region. A block resection of the tumor and involved sections of stomach, pancreas, and transverse colon was carried out, but the small portion in the region of the aorta had to be left *in situ*. The viscera were repaired, and the patient left the operating room in fair condition.

For the first 3 days after operation he held his ground, but on the fourth day he became jaundiced, developed unmistakable signs of bronchopneumonia and, in spite of heroic measures, expired the following morning, January 3, 1940.

At autopsy, a localized left upper quadrant peritonitis, infarct and gangrene of spleen, residual tumor, and bilateral lobular pneumonia were the principal findings.

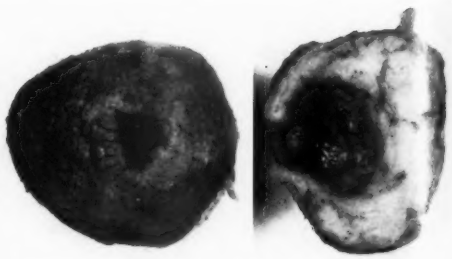

Fig. 8. Case 5. Malignant leiomyoma of stomach (6 by 5 by 4.5 cm.). An area of ulceration in the overlying mucosa opens into a central cavity surrounded by tumor tissue showing small foci of degeneration.

CASE 4. S. P. 59599. Unit Hist. No. 473180. J. A., a 49 year old white American male was admitted to the medical service of the Presbyterian Hospital on December 8, 1935, with a 4 years' history of indigestion, irregularly after meals, relieved occasionally by food and soda. For the previous 3 months he had experienced attacks of fullness and burning in the epigastrium, starting one hour after meals and occasionally at night. There was increasing weakness and 2 days before admission he had several tarry stools. On day of admission he experienced an attack of fainting.

There was pain and hyperesthesia over the lower sternum, anemia, elevated erythrocyte sedimentation rate and stool guaiac, ++++. He improved somewhat after being placed on a Sippy diet, but a barium series showed a smooth mass projecting forward in the posterior wall of the fundus of the stomach with a small crater shadow in its center. The tumor was considered to be either benign or a sarcoma, and the patient was transferred to the surgical service for operative treatment.

Operation on January 10. 1936. by Dr. Fordyce B. St. John, revealed a 6.5 by 4.5 by 4 centimeter endogastric, well circumscribed, firm, nodular tumor in the posterior wall of the fundus of the stomach. The overlying mucosa was ulcerated in 3 areas centrally, and the cut surface presented a glistening, "watered-silk" appearance, with areas of degeneration, cavitation, and hemorrhage directly beneath and continuous with the ulcerations (Fig. 4). No evidence of metastases was noted and a local resection of the mass was performed.

Microscopically, the tumor was composed of interlaced bundles and sheaves of oval or spindle-shaped smooth muscle cells, containing elongated palisaded vesicular nuclei. The cells were in the main fairly uniform in size, shape, and staining characteristics, but in one nodular area a group of closely packed, oval cells presented marked irregularity, with here and there a multinucleated form. Mitoses averaged 1 in every 3 high power fields. Myofibrils were not

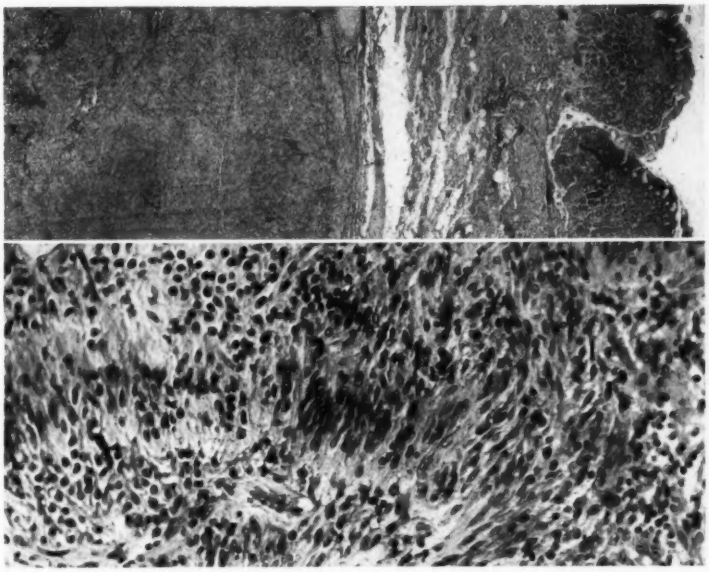

Fig. 9. Case 5. Malignant leiomyoma of stomach. The topography of the tumor is shown above. Below are the plump, closely packed smooth muscle cells with palisaded, vesicular nuclei and a scanty fibrous stroma.

demonstrated. In some places, at the margins, bundles of tumor cells interdigitated with strands of normal smooth muscle (Figs. 5 and 6).

Diagnosis: Malignant leiomyoma of stomach.

After operation the patient's course was very stormy. He developed a wound abscess, followed by subphrenic abscess and pyo-pneumothorax. These complications were treated surgically, but gastric and pleural fistulas remained. However, there was satisfactory slow improvement and he was discharged August 2, 1936, 207 days after operation. The fistulas gradually closed and, except for a ventral hernia, his general condition was quite satisfactory. At present, 5 years after operation, and 9 years after onset of symptoms, he is gaining weight and shows no evidence of recurrence.

Case 5. S. P. 72308. Unit Hist. No. 228716. C. S., a 45 year old white Irish male was admitted to the Presbyterian Hospital on October 22, 1939, with a 3 year history of repeated bouts of melena and hematemesis with progressive anemia. He was treated symptomatically for a supposed duodenal ulcer.

Physically, except for slight epigastric tenderness, no positive findings were elicited. A barium series was done and a large, rounded, smooth tumor was seen in the fundus of the stomach, attached by a broad pedicle to the posterior wall and projecting into the lumen. A crater which measured 2 centimeters was noted in the margin opposite the pedicle (Fig. 7).

Diagnosis: Malignant leiomyoma of stomach (Dr. Ross Golden).

Operation by Dr. Fordyce B. St. John on October 25, 1939, revealed a rounded, rather firm, endogastric tumor measuring 6 by 5 by 4.5 centimeters, arising in the posterior wall near the cardia. It was entirely covered by intact mucosa except in the central portion, where there was a 1.5 centimeter circular opening, with rounded, piled-up edges, leading directly into a 2.8 by 2.5 by 2 centimeter cavity. The walls of the latter were shaggy, rough, and grayish white, while the surrounding tissue was firm, homogenous, and reddish-gray. The main portion of the tumor was composed of glistening, grayish-white tissue arranged in irregular strands (Fig. 8). There was no evidence of metastasis. The mass was excised locally, and the stomach was closed. Recovery was entirely uneventful and the patient was discharged on the seventeenth day after operation. One year following operation, and 4 years after onset of symptoms, he is in excellent condition, with no complaints and no evidence of recurrence.

Microscopic examination revealed a highly cellular, fairly homogenous tumor made up of large elongated or spindle cells, with oval, vesicular nuclei arranged in palisades, and set in a scanty fibrous stroma. There was some variation in cellular and nuclear size and staining, with occasional mitotic figures (Fig. 9). Well defined myofibrils were seen in many places. There was no evidence of capsule formation, but the edges were fairly distinct and the

Fig. 10. Case 6. Roentgenogram of hour-glass leiomyoma of stomach. The endogastric portion makes an irregularly, rounded filling defect. Peristalsis was visualized fluoroscopically in the immediate vicinity.

Fig. 11. Case 6. Leiomyoma of stomach (hour-glass type). The larger portion (4.5 by 3.5 by 2.5 cm.) was endogastric. It is covered by flattened mucosa in which are crypt-like ulcerations. The smaller exogastric mass (2.8 by 2 by 1.8 cm.) is nodular and covered by serosa. The cut surface at the right shows areas of hemorrhage and necrosis.

tumor was entirely confined within the muscularis, except in the region of the ulceration.

Diagnosis: Malignant leiomyoma of stomach.

Case 6. S. P. 51874. Unit Hist. No. 384493. F. R., a 50 year old white Colombian female was admitted to the medical service of the Presbyterian Hospital, July 3, 1933, with a history of dyspnea and gas after meals, for many years. She also had had cramp-like right upper quadrant pains, but none in the past 2 years after an attack of jaundice. For the past 2 months she had become anemic and suffered with increased weakness and occipital headaches. Swelling of face and ankles and occasional vomiting occurred during the previous 2 weeks.

Physical examination revealed a definite pallor, tongue smooth at edges, and a moderately enlarged heart. There was tenderness in the region of the gall bladder. Stool guaiac, ++++. Roentgenography and fluoroscopy revealed a pedunculated mass arising from the posterior wall of the stomach just behind the cardiac orifice. Peristalsis was visible in the immediate vicinity (Fig. 10).

Diagnosis: Benign polyp of stomach (Dr. Ross Golden).

The patient was transferred to the surgical service and at operation on July 20, 1933, Dr. Fordyce B. St. John found an hour-glass tumor in the anterior wall of the stomach, high in the fundus, which he treated by simple local excision and gastrorrhaphy. There was no evidence of metastases. It was a firm, nodular mass, the endogastric portion measuring 4.5 by 3.5 by 2.5 centimeters, while the exogastric portion was 2.8 by 2 by 1.8 centimeters. The overlying mucosa was irregular and cryptic with several small sinuses extending into the mass and ending in an 8 by 4 millimeter cavity filled with a small amount of dried blood. Elsewhere the tumor tissue presented an indurated, grayish-white, occasionally whorled, cut surface containing scattered hemorrhages (Fig. 11).

Microscopically, the tumor was composed of irregularly interlaced bundles of spindle-shaped smooth muscle cells arranged as nodular whorls. Occasionally the tumor penetrated the muscularis mucosae. The nuclei in most places were elongated, often arranged in palisaded fashion, and myofibrils were scattered throughout. No mitotic figures were seen. The dense fibrous supporting stroma was moderate in amount, containing relatively few blood vessels, and there were many areas of serous degeneration. In some places a very thin fibrous capsule defined the tumor (Fig. 12).

Diagnosis: Leiomyoma of stomach.

The patient made an uneventful recovery and, when last seen in December, 1938, 7½ years after operation, her condition was excellent. She was lost to follow-up after that date.

Case 7. S. P. 68707. Unit Hist. No. 326714. J. B., a 44 year old British West Indies colored female was admitted to the Presbyterian Hospital on October 15, 1938, with a history of a slowly growing mass in the left upper quadrant during the past 4½ years. Recently there was a sensation of heaviness, but otherwise the tumor was entirely asymptomatic.

On examination, a freely movable, smooth, nontender 11.5 by 7 centimeter mass was palpable in the left upper quadrant. Percussion elicited tympany, anterior to the mass. Except for a lower midline scar of a previous appendectomy, there were no other remarkable findings. A barium series revealed a rounded tumor mass 6 centimeters in diameter projecting into the lumen from the anterior wall of the pars media (Fig. 13). Since the mass was also palpable anteriorly, it appeared that this was an hour-glass tumor arising within the stomach and, with a history of 4½ years' duration, it was considered a benign growth.

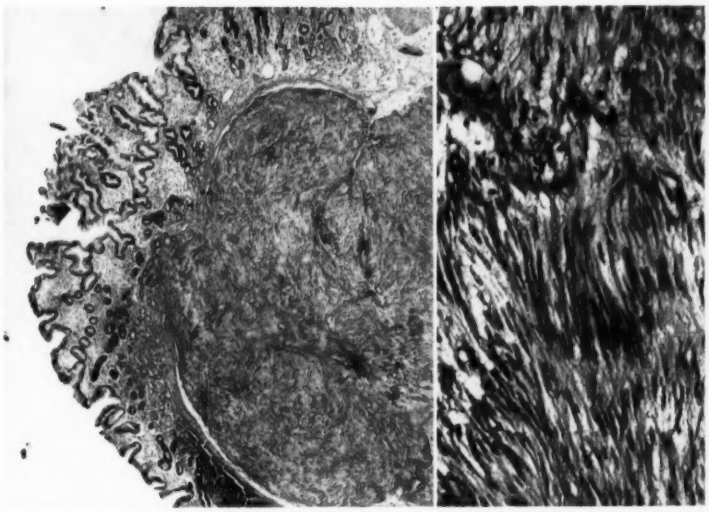

Fig. 12. Case 6. Leiomyoma of stomach (hour-glass type). The tumor is composed of interlaced bundles of smooth muscle cells and a fibrous stroma. It has broken through the muscularis mucosae (left). At the right are shown magnified tumor cells with some tendency to palisade their elongated nuclei.

Diagnosis: Leiomyoma of stomach (Dr. Robert P. Ball).

At operation, on October 21, 1938, Dr. Allen O. Whipple found a firm, hour-glass tumor originating in the anterior wall of the pars media, near the lesser curvature. The smaller endogastric mass measured 6 by 5 by 3.5 centimeters and was covered by intact, normal-appearing mucosa. The larger exogastric portion measured 12 by 8 by 6 centimeters, and the overlying serosa contained many tortuous, engorged blood vessels. Several dense adhesions extended from it onto the stomach (Fig. 14). On section there were many areas of degeneration, while in other places the tissue presented a grayish-white, "watered-silk" cut surface. There was no evidence of metastases. A partial gastric resection followed by a posterior Pólya gastroenterostomy was performed.

Microscopic examination revealed a well circumscribed tumor composed of whorled, interlaced bundles of highly differentiated, elongated, smooth muscle cells with palisaded nuclei. Many myofibrils were present and mitotic figures were very rare (Fig. 15). There was a moderate amount of poorly vascularized connective tissue stroma, arranged mostly as fibrous trabeculae and several areas of necrosis were seen.

Diagnosis: Leiomyoma of stomach.

The patient's recovery was uneventful and at present, 2 years following resection and 6½ years after the appearance of the tumor, her condition is excellent.

Case 8. Unit Hist. No. 72585. J. B., a 63 year old white American female was admitted to the medical service of the Presbyterian Hospital on July 11, 1928, with a 10 day history of indigestion and cramp-like epigastric pains. During the previous 2 days there were several tarry stools, together with nausea and hematemesis, as well as an attack of unconsciousness lasting 45 minutes. She lost 5½ pounds in the past year.

Physical examination revealed no positive findings except for secondary anemia and an elevated pulse. There was slight improvement with clyses and a transfusion, but on the seventh day there was sudden onset of deep shock, and the patient expired.

At autopsy (No. 10035), the stomach was found filled with a large amount of tarry mucoid material and in the posterior wall, 1 centimeter from the lesser curvature and 8 centimeters distal to the cardia, there was a stony-hard, well circumscribed, grayish-white, slightly exogastric mass measuring 2.3 by 2 centimeters. In the overlying mucosa there was an ulcer crater with raised edges, and clearly visible at the periphery were the openings of two blood vessels.

Microscopically, the tumor was composed of interlaced bundles of smooth muscle cells with elongated or oval, palisaded nuclei, and numerous myofibrils. No mitotic figures were seen. The fibrous stroma was scanty and vascularity was slight. It was partially surrounded by a very thin fibrous capsule and the center of the mass was occupied by a well defined area of degeneration with cavitation. At the edge of the shallow mucosal ulceration the open mouth of one of the eroded blood vessels was seen (Fig. 16).

Diagnosis: Leiomyoma of stomach (degeneration and erosion of gastric blood vessels).

Fig. 13. Case 7. Roentgenogram of hour-glass leiomyoma of stomach (diagnosis made preoperatively). The endogastric component of the tumor makes a smooth, rounded filling defect near the cardia, while the exogastric portion is suggested by the distortion of the lesser curvature.

Duodenum

CASE 9. Unit Hist. No. 352745. Autopsy No. 11053. (Previously reported by Andersen and Doob (1933). J. O., a 37 year old white American male

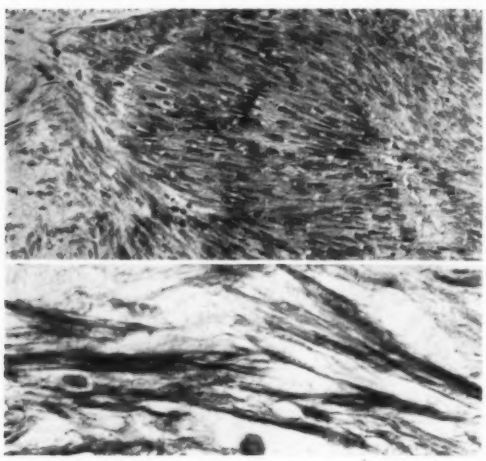

Fig. 15. Case 7. Leiomyoma of stomach (hour-glass type). The tumor is made up of interlaced bundles of smooth muscle cells with palisaded nuclei and well developed myofibrils shown magnified below.

Fig. 14. Case 7. Leiomyoma of stomach (hour-glass type). The posterior wall of the stomach has been removed showing the pylorus at the right and the bilobed tumor high on the lesser curvature. The smaller endogastric portion covered by smooth mucosa measures 6 by 5 by 3.5 centimeters. The larger exogastric part covered by serosa with dilated veins is 12 by 8 by 6 centimeters.

was admitted September 14, 1932, with a 5 weeks' history of tarry stool, weakness, pallor, loss of weight, shortness of breath and a right-sided abdominal mass. He also had swelling of the feet and ankles, especially the right, and a severe "squeezing" pain in the right leg for the past 8 days. He had been hospitalized 5 years previously for similar, although less severe, complaints and at that time a diagnosis of duodenal ulcer was made. There was no evidence of this by roentgenogram, but he improved on a Sippy diet and liver therapy. In the intervening years he had repeated gastric hemorrhages, but recovered from each.

Physical examination revealed an acutely ill, anemic young male, with elevated temperature. A slightly tender mass in the right upper abdomen extended 3 to 4 centimeters below the liver edge. It was indurated, irregular, well circumscribed, and apparently attached to the retroperitoneal tissue. A barium series showed this mass to be apparently outside the gastrointestinal tract. On September 18, he had a fainting attack and on the 20th, while on a bed pan, he felt weak, dizzy, and gasped for air. He passed a large tarry stool, went into extreme shock, and died shortly thereafter.

At autopsy, the mass occupied the center of the abdominal cavity, compressing the overlying bowel. It extended slightly more to the right and was adherent to the capsule of the lower pole of the right kidney. It was adherent to, and pulled the duodenum down to the level of, the lower lumbar vertebrae. It measured 18 by 15 by 12 centimeters, with

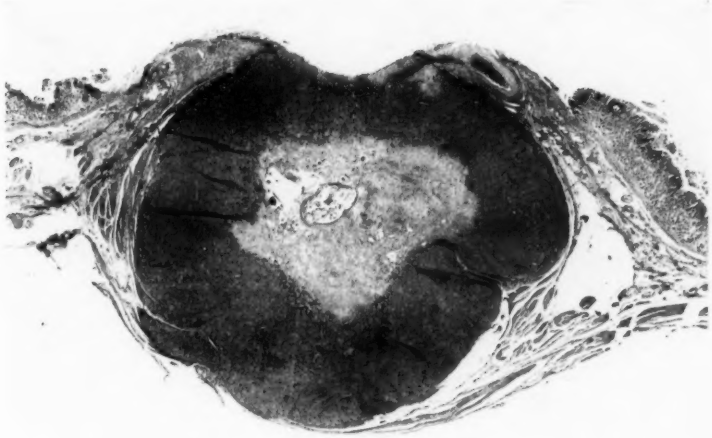

Fig. 16. Case 8. Leiomyoma of stomach. The 2 centimeter tumor expands the muscular coat, and ulceration through the mucosa has excavated it superficially. The ulceration also eroded two large submucosal blood vessels and caused fatal hemorrhage. One is shown adjoining the tumor.

central degeneration and cavitation communicating with the duodenum by a 3 centimeter opening at the level of the ampulla of Vater. It compressed the inferior vena cava and was in contact with the head of the pancreas, but did not invade it. Three nodules, the largest measuring 5 centimeters in diameter, were found in the liver, and the immediate cause of death was thrombosis of the common iliac veins with pulmonary embolism.

Microscopically, the tumor was composed of interlaced bundles of smooth muscle cells with elongated, palisaded nuclei showing variation in size, shape, and staining. Myofibrils were occasionally seen and mitoses were uncommon. There was a moderate amount of fibrous stroma containing few blood vessels. The mass was rather well circumscribed, and the overlying mucosa was everywhere intact, except in the region of the sinus tract. The nodules in the liver were made up of similar tissue.

Diagnosis: Malignant leiomyoma of duodenum, with metastases to liver. Thrombosis of common iliac veins. Embolism of pulmonary arteries.

Case 10. Unit Hist. No. 530590. Autopsy No. 12666. C. S., a 53 year old white German male was admitted January 7, 1938, with a history of generalized abdominal pain for 9 hours and fecal vomiting for 7 hours. Onset of illness 3 months previously with exertional dyspnea, ankle edema, afternoon fever, and intermittent lower abdominal, cramping pain.

Examination revealed an acutely ill, markedly anemic patient with generalized abdominal tenderness and rebound tenderness; marked distention, tympany around diaphragm, and flatness in the flanks; no fluid waves. Stool guaiac, ++++. A flat plate showed intestinal ileus. He went rapidly downhill and died within 3 hours.

Clinical diagnosis: Mesenteric thrombosis. Bacterial endocarditis.

Fig. 17. Case 9. Malignant leiomyoma of jejunum (hourglass type). The tumor interdigitates with the fibers of the muscularis from which it arose. The picture does not show the ulceration in the larger endoenteric portion. Three areas of calcification are shown.

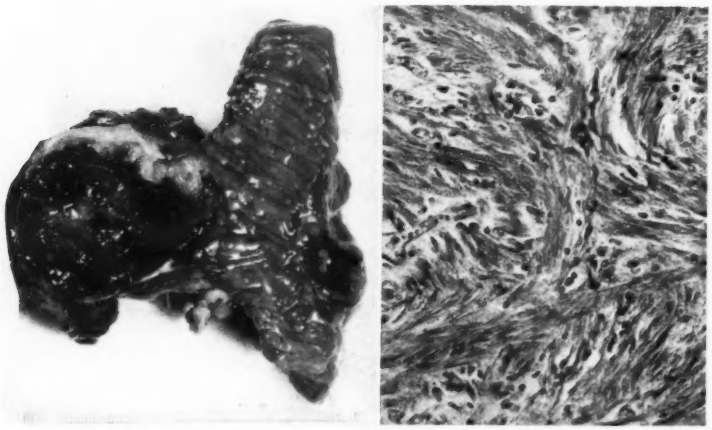

Fig. 18. Case 14. Leiomyoma of ileum (6 by 6 by 5 cm.). The gut and tumor have been bisected longitudinally. A mucosal ulceration leads into a 2.5 centimeter cavity. Most of the tumor is exoenteric. It is composed of interlaced bundles of relatively well differentiated smooth muscle cells and fibers.

At autopsy, a large, fluctuant retroperitoneal mass lay between the bifurcation of the aorta below and the postero-inferior border of the stomach above, reaching laterally to both renal pelves. The central portion was filled with foul, hemorrhagic, necrotic, friable material, and communicated with the lumen of the dilated descending portion of the duodenum via a 7 by 5 centimeter perforation in its postero-lateral aspect. The horizontal and ascending portion of the duodenum, as well as the pancreas, appeared to be incorporated within the mass, and the pancreas itself could not be identified. Posteriorly, the mass lay anterior to the inferior vena cava and abdominal aorta, but neither was involved. There was an acute diffuse fibrinopurulent peritonitis with 500 cubic centimeters of serosanguineous fluid from which Streptococcus viridans and Bacillus coli were cultured, but no definite point of perforation of the mass could be identified. No evidence of regional or distant metastases was found. The heart showed evidences of aortic stenosis with insufficiency and enlargement.

Fig. 19. Case 15. Malignant leiomyoma of Meckel's diverticulum. The degenerated, hemorrhagic tumor (13 by 11 by 8 cm.), arising at the tip of the diverticulum, caused torsion and complete obstruction of the ileum.

Microscopically, the tumor was composed of well differentiated, uniform, elongated smooth muscle cells with palisaded nuclei and a moderate amount of fibrous stroma. Definite myofibrils were noted throughout, and no mitoses were seen. Vascularity was poorly developed, and there were many areas of degeneration and necrosis.

Diagnosis: Leiomyoma of the duodenum. Acute diffuse peritonitis. Pancreatic fat necrosis. Acute rheumatic endocarditis. Aortic stenosis and insufficiency.

Jejunum and Ileum

Case 11. P. & S. No. 12564. P. S., a white American male, aged 60, was admitted to St. Luke's Hospital, Utica, New York, on July 2, 1932, with a 3 days' history of tarry diarrhoea and fainting spells associated with weakness. Previous general health had been very good: average weight, 168 pounds and he had gained during last 2 years. There was no definite evidence suggestive of ulcer or acute abdominal catastrophe and, except for an evident anemia, the physical examination brought to light no positive findings.

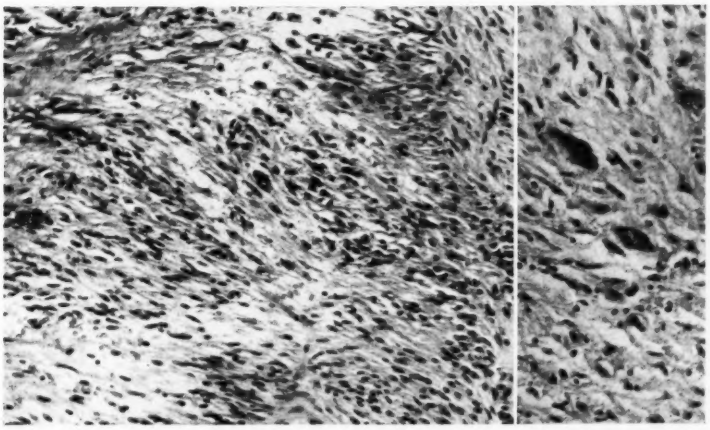

Fig. 20. Case 15. Malignant leiomyoma of Meckel's diverticulum. The cells are arranged in bundles and vary considerably in size. Some bizarre forms are enlarged at the right.

He was observed for 2 weeks and given 3 small transfusions. At the end of that time his stools were normal in color and he was discharged. During the following 4 days he again had tarry stools on two occasions and was readmitted. After 1 week there was no further evidence of intestinal hemorrhage, and he was again discharged. In the ensuing 2 weeks a barium series was reported negative, but the following week the tarry stools returned, he was again admitted to the hospital, and after a 2 week period, during which he received 6 transfusions, exploratory laparotomy was decided upon.

Operation was done by Dr. C. S. Dickson, on August 31, 1932. An ovoid, firm, elastic "hour-glass" tumor about the size of a pecan nut was found in the antimesenteric aspect of the jejunum 2 feet distal to the duodenaljejunal flexure. A 6 centimeter section of jejunum, including the tumor, was resected, followed by end-to-end anastomosis. The mass was covered by normal mucosa, except at the apex, where there was an oval ulceration 1.5 by .6 centimeters with well defined margins and evidently the site of hemorrhage. On section the cut surface presented a grayish-white, translucent sheen dotted by small hemorrhages.

Microscopically, the tumor was made up of large smooth muscle cells with elongated oval nuclei, arranged in interlaced bundles. There was some variation in size and shape, but mitoses were rare. Material for special stains was not available and myofibrils could not therefore be demonstrated. The connective tissue stroma was moderate in amount, rather vascular, and in several places there were small foci of calcification. There was no well defined capsule and at several points tongues of less well differentiated tumor tissue interdigitated with the normal muscularis (Fig. 17).

Diagnosis: Malignant leiomyoma of jejunum.

The patient made an uneventful recovery and is in excellent health 8 years following operation.

Case 12. S. P. 66463. Unit Hist. No. 537691. A. M., a 68 year old white female admitted with a 3 months' history of sensation of weight in lower abdomen with increasing constipation. There was an abdominal mass with evidence of intestinal obstruction and an exoenteric malignant leiomyoma of the ileum was found, but could not be removed. She died 8 months after operation, 11 months after onset of symptoms. Autopsy was not permitted.

Case 13. S. P. 68023. Unit Hist. No. 514500. S. M., a 49 year old white male was admitted with severe intestinal hemorrhage and marked secondary anemia, treated unsuccessfully over a period of 3¼ years. A 7.5 centimeter hour-glass malignant leiomyoma of the distal ileum was resected, and the patient has been in good health for 2½ years, approximately 6 years following onset of symptoms.

Case 14. S. P. 64503. Unit Hist. No. 516225. J. L., a 30 year old white Italian male, was admitted to the Presbyterian Hospital on July 1, 1937, with a 6 months' history of left lower quadrant aching pain, gradual in onset, but constant and associated with increasing constipation.

Examination revealed moderate midline spasm and tenderness, as well as a slightly tender, firm, movable mass in the left lower quadrant. A barium series revealed only a slow emptying of the ileum.

An exploratory celiotomy on July 9, 1937, by Dr. C. L. Janssen, revealed an exoenteric, nodular tumor attached to the wall of the ileum at the junction of the middle and distal thirds. It measured 6 by 6 by 5 centimeters and on section it was grayish-pink, rubbery, and projected slightly endoenterically. There was a 2.5 centimeter central cavity with a 5

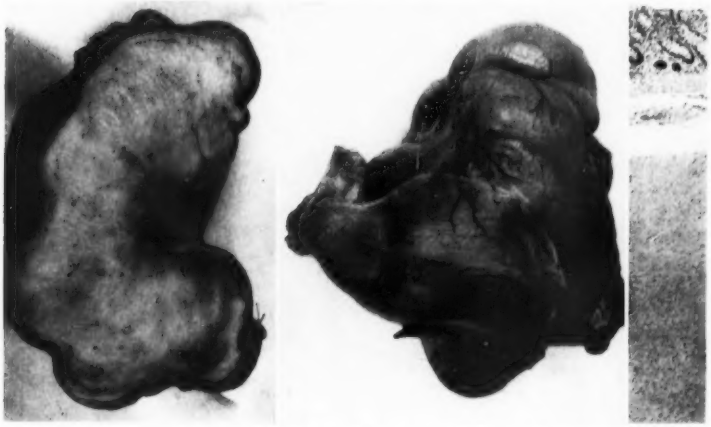

Fig. 21. Case 17. Leiomyoma of descending colon. The nodular tumor (9.5 by 5.5 by 5 cm.) is covered by a veil of mesentery and lies behind the involved loop of bowel, which here extends from left to right. The portion overlying the tumor is flattened and widened. Cross section illustrates the glistening "watered-silk" cut surface. The flattened lumen of the colon is seen at the left. The tumor is made up of well differentiated cells and myofibrils (right).

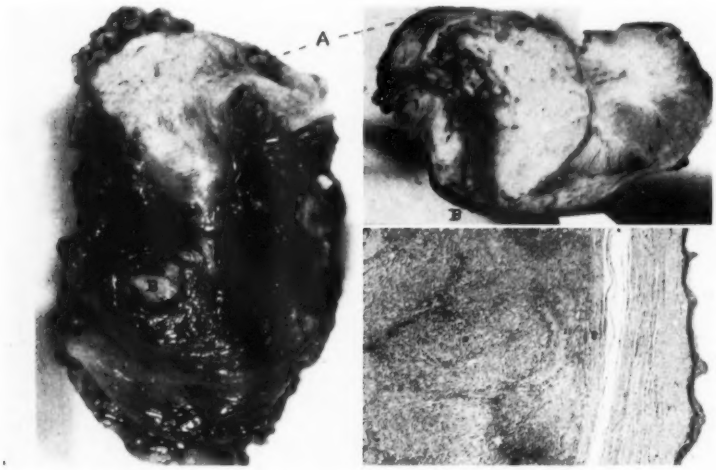

Fig. 22. Case 18. Malignant leiomyoma of rectum. The 4 centimeter tumor projects into the rectum and causes a slight bulge in the posterior vaginal wall, *A*. A cavity in the tumor due to necrosis opens into the rectum at *B*. The detail shows the approach of the tumor to the vaginal mucosa.

millimeter tract leading into the bowel lumen. No metastases were seen (Fig. 18). A partial enterectomy with end-to-end entero-enterostomy was performed, but the patient had a stormy postoperative course. On the fourth day his wound disrupted, he went rapidly downhill, and expired the following morning. There was no autopsy.

Microscopically the poorly delimited tumor showed well differentiated smooth muscle cells in interlaced bundles, with scanty, poorly vascularized fibrous stroma. Many myofibrils were noted, mitoses were rare. Centrally, degeneration and cavitation with ulceration of overlying mucosa (Fig. 18).

Diagnosis: Leiomyoma of the ileum.

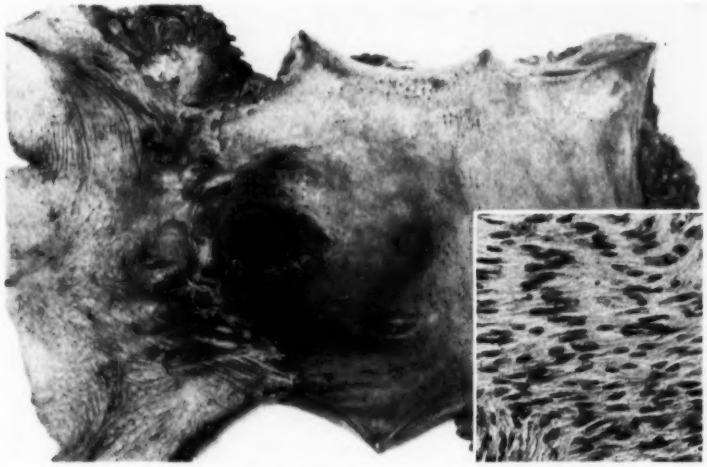

Fig. 23. Case 19. Malignant leiomyoma of rectum. The 5.5 by 5 by 4.5 centimeter tumor bulges forward from the posterior wall and the ulceration in the lower portion resulted from the biopsy. The inset shows the large, plump smooth muscle cells with elongated, palisaded nuclei.

Meckel's Diverticulum

Case 15. S. P. 60740. Unit Hist. No. 244795. J. G., a 33 year old white French female was admitted to the gynecological service of the Presbyterian Hospital on April 23, 1936, for uterine bleeding following an abortion 14 weeks previously. On the day following a dilatation and curettement of the uterus, she developed acute distention, nausea, vomiting, fever, oliguria, jaundice, and a mass appeared in the left upper quadrant. There was also diffuse abdominal pain. She was transferred to the surgical service and on May 7, 1936, Dr. Rudolph Schullinger, suspecting an acute ileus due to pelvic peritonitis, did an exploratory laparotomy. He found a diverticulum of the ileum 4 feet from the ileocecal junction, covered by omentum and involved in a mass measuring 13 by 11 by 8 centimeters. This was for the most part necrotic, friable, and ecchymotic, while at the tip of the diverticulum, which was embedded in the mass, the tissue was pinkish-white and rather homogeneous. The mass had caused a torsion in the bowel, obstructing its lumen (Fig. 19) and was resected with the diverticulum and 25 centimeters of ileum, followed by a side to side ileo-ileostomy.

Microscopically, the tumor apparently originated in the muscularis of the diverticulum. It was almost entirely encapsulated by a layer of peritoneum and composed of interlaced bundles of smooth muscle cells with rather irregular, elongated nuclei and scattered myofibrils. Occasional bizarre forms were seen, but mitoses were exceedingly rare. The stroma was scanty, but highly vascularized. In many places there was hemorrhage and degeneration (Fig. 20).

Diagnosis: Malignant leiomyoma of Meckel's diverticulum.

The patient developed a pulmonary infarct with pneumonitis on the ninth day after operation and a phlebitis of the left leg on the eighteenth day, but recovered satisfactorily, and was discharged in good condition on the thirtieth day. At present, 4½ years following operation, she is alive and well, with no evidence of recurrence.

Colon

Case 16. P. & S. 15225. Army Medical Museum No. 54461. Sections of a malignant leiomyoma of

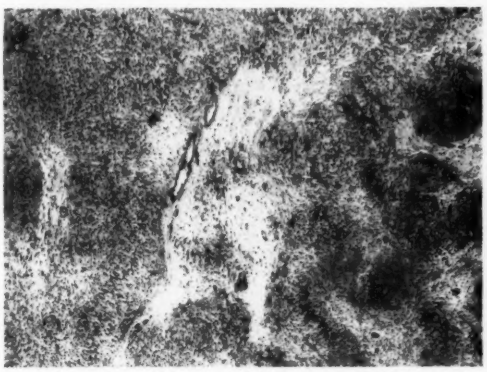

Fig. 24. Case 31. Leiomyoma of stomach. The section illustrates a striking resemblance to a neurilemmoma. The closely packed, palisaded nuclei are interspersed with areas of loosely arranged, degenerated stroma, thus imitating the differentiation into A and B tissue of a neurilemmoma. The myofibrils in this tumor indicated smooth muscle origin.

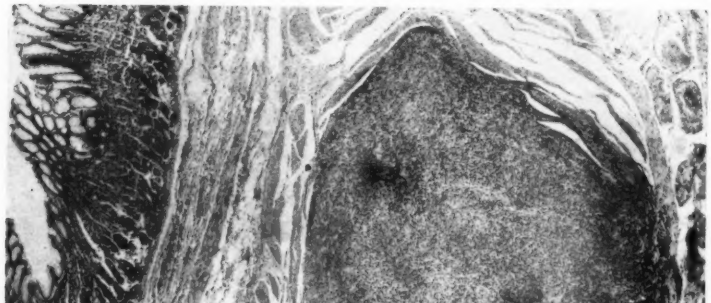

Fig. 25. Case 32. Leiomyoma of stomach. This was an incidental finding in a stomach resected for duodenal ulcer. It lies entirely within the external layer of muscle with which it interdigitates.

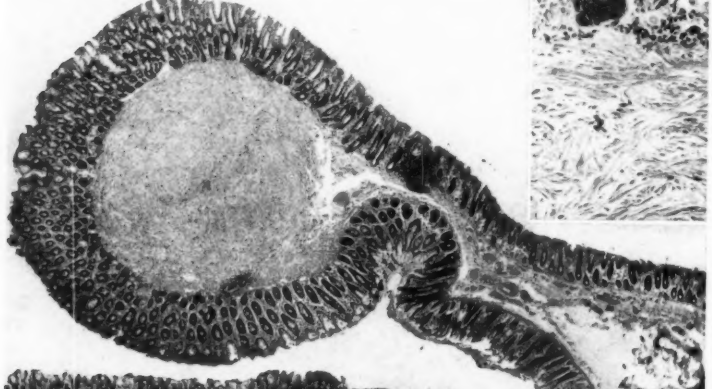

Fig. 26. Case 36. Pedunculated leiomyoma of sigmoid colon. The 15 by 15 millimeter tumor lies in the submucosa in continuity with the muscularis mucosae and entirely separated from the muscularis. The detail shows its well differentiated cells and myofibrils.

the sigmoid colon were submitted by Major Elbert DeCoursey, M. C.

The patient was a 78 year old white male who had an abdominal mass and slight intestinal hemorrhage for 6 months. The tumor was about the size of a 6 months' fetus and 1 year after its removal his condition was entirely satisfactory.

CASE 17. S. P. 62450. Unit Hist. No. 503207. H. F., a 47 year old white American female was admitted to the Presbyterian Hospital on November 11, 1936, complaining of intermittent severe attacks of cramping left lower quadrant pain of 4 years' duration, coming on every 6 to 8 weeks and lasting 24 hours. They were associated with nausea, vomiting, and constipation, alternating with obstipation.

Examination revealed a firm, tender, deep, immovable orange-sized mass high in the left lower quadrant. A barium series, done elsewhere, revealed an "extra loop of bowel."

At operation, on November 16, 1936, Dr. Allen O. Whipple found a nodular, exocolonic tumor partially obstructing the lumen of the descending colon. It was kidney-shaped, measured 9.5 by 5.5 by 5 centimeters, and on section presented a rubbery, semitranslucent, pinkish-white, glistening "watered-silk" cut surface. There was no evidence of metastases. The lumen of the bowel in this region was markedly flattened and widened, while the uninvolved portion was somewhat narrowed (Fig. 21). The mass, with 9.5 centimeters of large bowel, was resected, followed by end-to-end anastomosis.

Microscopically, the tumor was made up of well differentiated smooth muscle tissue with abundant fibrous stroma. It was well circumscribed, lying just beneath the muscularis mucosae. Numerous myofibrils were seen and there were no mitoses (Fig. 21).

Diagnosis: Leiomyoma of descending colon.

Convalescence was uneventful and at present, 4 years after operation and 8 years after onset of symptoms, the patient is in good condition, showing no evidence of recurrence.

Rectum

CASE 18. S. P. 65922; 66089; 74094. Unit Hist. No. 538227. M. R., a 51 year old white American female was admitted to the Presbyterian Hospital on December 20, 1937, with a history of rectal bleeding, tenesmus, and much gas for 2 weeks. The bleeding was quite marked and resulted finally in extreme weakness.

Examination revealed a moderate anemia and a well defined tumor mass in the lower rectum. It was pale pink, finely lobulated and measured 4 centimeters in diameter. The overlying mucosa was ulcerated, and there was central cavitation. The mass bulged slightly into the rectal lumen and extended into the posterior wall of the vagina, but was without mucosal involvement.

Several small pieces of tissue were passed spontaneously and examination of these revealed whorled masses of closely packed, large spindle shaped cells arranged in interlaced bundles. The nuclei were elongated, blunt-ended, and varied somewhat in size and shape. Occasional mitoses were noted, but no myofibrils could be demonstrated.

A diagnosis of malignant leiomyoma of the rectum was made and on January 13, 1938, Dr. C. L. Janssen removed the mass (Fig. 22) by wide excision involving a partial colpectomy and proctectomy with establishment of a permanent colostomy.

Microscopic sections (Fig. 22) were similar to the previous ones. The tumor was rather well preserved and sharply circumscribed, except at the proximal cut edge. Here, there was an area of extension outside of the main tumor mass alongside of a vein and it was feared that this might be responsible for reappearance of the tumor. The vaginal mucosa was closely approached, but no invasion was seen.

The patient's convalescence was uneventful, and she was discharged in good condition, but within several months there was a recurrent nodule measuring 1.75 centimeters in diameter in the operative site. This was widely excised on April 18, 1940, 2 years after the first operation, and proved to be similar to, but less well preserved than, the original tumor. At present, 8 months after the last excision, and 3 years following the onset of symptoms, she is well, showing no evidence of further recurrence.

CASE 19. S. P. 74371; 74404. Unit Hist. No. 610051. E. J., a 59 year old white American male was admitted to the Presbyterian Hospital on May 10, 1940, complaining of sacral pain and a mass in the rectum of 1 year's duration. The stool had decreased in caliber in the last 2 to 3 months and he had lost 18 pounds in weight, but explained the latter on the basis of severe grief for his wife's recent death. The pain began at the base of the spine and radiated to the left hip and knee.

Examination revealed a firm, non-tender rectal mass measuring 5.5 by 5 by 4.5 centimeters. It was situated just above the crypts of Morgagni in the posterior wall, and bulged into the lumen about 2.5 centimeters. The overlying mucosa was flattened but intact. Just below the mass there was a 2 centimeter external hemorrhoid and another smaller one was seen in the anterior midline (Fig. 23). A diagnosis of malignant leiomyoma of the rectum was made and substantiated by biopsy, taken on the day after admission.

On May 14, 1940, a colostomy with perineal proctectomy was performed by Dr. C. L. Janssen and recovery was uneventful.

Microscopic sections of the tumor showed interlaced bundles of large, plump smooth muscle cells, with elongated palisaded nuclei. Myofibrils were seen occasionally and no mitoses were noted. The fibrous stroma was scanty, relatively avascular and the overlying mucosa was intact (Fig. 23).

Diagnosis: Malignant leiomyoma of the rectum.

The patient is in excellent health at present, 6 months after operation and 1½ years following onset of symptoms. There is no evidence of recurrence, but the elapsed time since operation is still too short for adequate evaluation of his course.

CASE 20. S. P. 46846; 48387. Unit Hist. No. 318864. Autopsy No. 10970. A. S., a 64 year old white male was admitted with a rectal tumor of 3 years' duration. No hemorrhage. He died 2 days after a preliminary colostomy was performed and autopsy showed an exorectal malignant leiomyoma 11 centimeters in diameter. Death was caused by a marked urinary infection.

CASE 21. P. & S. 7872. (Courtesy of Dr. William Brandes, Roosevelt Hospital). W. P., a 61 year old white Scotch male, was admitted to Roosevelt Hospital on July 20, 1922, complaining of a rectal mass. It began as a small growth 8 months previously and had grown rapidly, attaining the size of a plum. It protruded during defecation and caused urgency and constipation. His general health was satisfactory. The tumor was attached by a 2.5 by 1 centimeter pedicle to the left lateral aspect of the rectum and measured 6 centimeters in diameter. It was irregular, indurated, and partially covered by a necrotic, greenish-gray membrane. Opposite this mass were several small, hard, sessile nodules, each about the size of a large black-headed pin.

On July 22, 1922, under a diagnosis of "polypoid tumor of rectum." Dr. J. I. Russell excised the mass through its pedicle. The other nodules were noted, but not treated, and were to be observed periodically.

Microscopically, the tumor was composed of interlaced bundles of rather well differentiated smooth cells in a scanty fibrous stroma, showing a moderate amount of degeneration. Occasional mitoses were seen and there was variation in cellular size and shape. Special stains for demonstrating myofibrils were not available.

Diagnosis: Malignant leiomyoma of rectum.

Patient was discharged in good condition on the ninth day after operation, but he was lost to follow-up after his discharge and it is not possible to comment on his subsequent course or the fate of the rectal nodules which were not removed.

CASE 22. S. P. 50748. Unit Hist. No. 366781. Autopsy No. 11628. A. W., a 67 year old white male was admitted with symptoms of an enlarged prostate. During prostatectomy a 5 centimeter leiomyoma of the rectum was also found and enucleated. One and one-half years later he died of chronic bronchitis with bronchiectasis.

Retroperitoneal Tissues and Mesentery

CASE 23. S. P. 54932. Unit Hist. No. 421725. L. E., a 39 year old white female was admitted for treatment of abdominal swelling, weakness, and epigastric pain, present for 2 years. A retroperitoneal malignant leiomyoma with metastases to the liver was found and a biopsy specimen only removed. When last heard from, 6 months after operation, she was bedridden, and death appeared imminent.

CASE 24. S. P. 40011. Unit Hist. No. 79613. E. T., a 57 year old white American female was admitted to the Presbyterian Hospital on March 12, 1929, with a 5 year history of loss of appetite and strength, together with a weight loss of 59 pounds. Two years previously she began to have attacks of cramp-like abdominal pains accompanied by gaseous eructations and bloating. Pain radiated to the umbilicus and flanks and was most severe in right lower quadrant. There was marked constipation. Symptoms increased in severity in past few months and were accompanied by distention.

Examination revealed a hard, firm, nodular mass in the medial aspect of the right lower quadrant. There was moderate anemia. A barium series showed a partially calcified abdominal mass and diverticulosis of descending colon and sigmoid.

On March 12, 1929, Dr. William Barclay Parsons excised this mass. It was firm, lobulated, and measured 12 by 8 by 6 centimeters, apparently originating in retroperitoneal tissue in the right lumbar region. The right ureter was encircled between two lobules of the tumor. The cut surface was gray, partially translucent, and more or less uniform.

Microscopic examination revealed interlaced strands of uniform smooth muscle cells in which myofibrils could be identified. Mitoses were rare. The relatively avascular stroma was scanty and many large areas of degeneration were noted.

Diagnosis: Leiomyoma of retroperitoneal tissue.

Recovery was uneventful and patient gained 50 pounds in the following year. For 4 years her condition remained good, then her symptoms returned. She returned to the hospital and the genitourinary service found a recurrent mass attached to the lower pole of the right kidney, as well as the psoas fascia and scar of previous operation. On November 3, 1933, Dr. George Cahill removed the kidney with the mass, but the kidney contained no tumor tissue. The tumor closely resembled the original. About 3 months later, on January 20, 1934, Dr. Parsons explored her again and found marked extension into and around the terminal aorta with numerous metastatic nodules in the liver. A biopsy (S. P. 53298) taken at that time revealed no further evidence of malignancy, but in view of the rapid recurrence and metastases, the final diagnosis had to be changed to malignant leiomyoma of retroperitoneal tissue with metastases to liver.

Patient went steadily downhill and expired December 11, 1934, 5½ years after the first operation and 10½ years after onset of symptoms. No autopsy could be obtained.

CASE 25. S. P. 69790. Unit Hist. No. 570124. J. D., a 60 year old white female was admitted with a 4 year history of a left-sided, slowly growing abdominal mass. A retroperitoneal, malignant leiomyoma with metastases to the peritoneum was found and biopsied only. The tumor grew rapidly following the operation and she expired 1 month later. An autopsy could not be obtained.

CASE 26. S. P. 35101. Unit Hist. No. 66636. Autopsy No. 9838. H. P., a 70 year old white male was admitted with symptoms of enlarged prostate for 5 years. During prostatectomy a retroperitoneal malignant leiomyoma was also found. An attempt at removal was made 1½ months later, but he ex-

pired 4 hours after this second operation. Autopsy revealed a gangrenous cystitis.

CASE 27. P. & S. 17470. M. S., a 66 year old white female had recurrence of a retroperitoneal malignant leiomyoma which had been excised 5 years ago. The tumor was again removed, but only incompletely, and within 3 months of the second operation there was another recurrence. At present, 6 years after the first operation and 9 months after the second, she is failing rapidly.

CASE 28. S. P. 58557. Unit Hist. No. 463624. A. C., a 52 year old white female was admitted with a 1 year's history of intermittent left upper quadrant abdominal pain and a mass. A retroperitoneal malignant leiomyoma was found, but could only be biopsied. She died 24 hours after operation of an undetermined cause. No autopsy.

CASE 29. Unit Hist. No. 35248 (Neurological Institute). Autopsy No. 12641. R. *Z.*, a 32 year old white American male was admitted to the Neurological Institute on October 4, 1937, complaining of pain in left lumbar region, constipation, impotence, weakness of both lower extremities and lower abdominal muscles and swelling of feet and legs for eight months. There were also bladder disturbances. In September he had had a spinal tap in Arizona, following which he became unable to make use of his lower extremities.

Examination revealed almost complete paraplegia of the lower extremities with loss of sensation up to first lumbar on the right and eleventh thoracic on the left. There was edema of the feet and ankles, marked atrophy, and severe sacral decubitus with lesser ulcerations on both hips. Temperature ranged from 99 to 104 degrees F. Roentgenogram findings were strongly suggestive of an extradural sarcoma involving twelfth thoracic and first lumbar vertebrae. Patient was treated by roentgenotherapy, but developed a pyelonephritis, became comatose, and expired December 17, 1937, 10 months following onset of symptoms.

At autopsy, a large lobulated tumor mass was found in the left retroperitoneal region, firmly attached to, and invading the left psoas muscle, as well as the first, second, and third lumbar vertebrae. There was a curious extension into the inferior vena cava by an isthmus of tumor tissue across the vertebrae and projecting into the vena cava. It apparently did not completely obstruct the lumen. On section, a firm whitish, whorled cut surface was seen.

Microscopically, the tumor was made up of well differentiated, uniform, interlaced smooth muscle cells containing palisaded elongated nuclei. Numerous myofibrils were present and mitoses were rare. There was a moderate amount of fibrous stroma.

Diagnosis: Leiomyoma of retroperitoneal tissue.

CASE 30. S. P. 52994. Unit Hist. No. 398006. R. M., a 44 year old white Irish female was admitted to the gynecological service of the Presbyterian Hospital complaining of vaginal bleeding for 27 days, and a fixed, circumscribed, slightly tender mass in the right lower quadrant for six months.

Examination revealed that the mass extended from the umbilicus to the pelvis. Cystoscopy and roentgenography showed a right hydronephrosis due to a mass extrinsic to the gastrointestinal tract.

On December 12, 1933, following dilatation and curettement of the uterus, Dr. Allen O. Whipple found an indurated, fibrous mass involving a large portion of the mesentery of the ileum and the ileocolic vessels. It measured 10 by 8 centimeters, and the transverse colon was adherent to it. It bled easily and was considered inoperable, so that only a biopsy was taken.

The biopsy specimen was composed of a few well differentiated smooth muscle cells in an abundance of poorly vascularized connective tissue stroma. The cells were quite uniform and myofibrils were rare, but no mitoses were seen.

Diagnosis: Leiomyoma of mesentery of ileum.

The patient made a satisfactory recovery and it was decided to try roentgenotherapy on the mass, but it apparently decreased in size somewhat, much to the surprise of observers, and treatment was refused by the patient. Her condition continued satisfactory and at present, 7½ years after appearance of the mass, she is in good health, employed as a domestic. The tumor appears definitely smaller, and remains entirely symptomless.

SUMMARY

1. Smooth muscle tumors occur throughout the entire gastrointestinal tract and often in the retroperitoneal tissues. They are found most commonly in the stomach and their incidence in general is much higher than suspected.

2. Classification of the tumors into benign and malignant is difficult because frequently poorly differentiated ones, which have the histological criteria of malignancy, do not display its clinical evidences, while occasionally a well differentiated tumor has grown by infiltration and metastasized. The terms leiomyoma and malignant leiomyoma are preferred to any others proposed. However, such classification has not been based solely upon histological criteria, but has been modified occasionally by biological behavior.

3. Early diagnosis is seldom accomplished, but if the possibility of such a tumor is kept in mind, more of these cases will be benefited by early treatment before secondary complications determine a less favorable prognosis. The presence of this type of tumor should be suspected, especially in all cases of gastrointestinal hemorrhage if the origin has not been determined.

4. Surgery is the only method of treatment and in many instances must be of a radical nature.

5. Prognosis is as much dependent upon the anatomical site of the tumor as upon its histological character. Tumors of the stomach, jejunum, ileum, and colon are restrained for a long time by the barrier of the peritoneum so that they can be entirely removed, usually with success. The anatomical peculiarities of the duodenum, the rectum, and the retroperitoneum make the complete removal of their tumors more difficult and sometimes impossible. For this reason recurrence following attempted surgical removal has been more frequent and the prognosis therefore much less favorable.

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DYSGERMINOMA OCCURRING IN A PSEUDOHERMAPHRODITE

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PRIOR to the important work of Robert Meyer in rationalizing the classification of ovarian neoplasms, numerous confusing terms were applied to the new-growth known at present as dysgerminoma ovarii. Because of variations in its histological structure, this tumor had been described variously by pathologists and clinicians as embryonal carcinoma, carcinosarcomatodes, giant cell sarcoma, embryoma, alveolar large cell carcinoma, and round cell sarcoma. It was reported in the female first by M. Chenot who, in 1911, described an ovarian tumor which he called "seminoma," because he thought it was derived from the anlage of seminiferous tubules. A year later, Pick reported the same tumor as "chorioepithelioma ectodermale" and postulated that it was derived from cells of chorionic villi. In 1931, Robert Meyer wrote that he had begun collecting cases "a long time ago," and had found 27 examples in hermaphrodites and pseudohermaphrodites, and 21 in otherwise normal females. It was his important observation, that this and others of the ovarian tumors have definite relationship to the hormonal activity of the gonads, which gave new impetus to the study of ovarian neoplasms. He rejected the name "seminoma" because there is no tendency toward masculinization, and suggested the term "dysgerminoma" because of the frequent appearance of the tumor in pseudohermaphrodites and in female subjects with poorly developed genitalia.

HISTOGENESIS

Following Meyer's effort to classify tumors of the ovary on the basis of their hormonal effect, other investigators studied more carefully the histogenesis of the ovary in an attempt to correlate the new clinical concepts with the morphological findings in the developing gonad. Ewing and Meigs, among others, developed the concept that dysgerminoma represents a one-sided development of a teratoma. Geist contended that the neoplasm springs from sexually undifferentiated cells developed from the surface epithelium of the anlage of the ovary. Schattenberg and Harris (17, 18), Chaney and Greenblatt, Novak and Gray, together with Meyer believed that dysgerminomas arise from cell rests, which are left over from that stage in gonadal development in which there is no sexual differentiation and which subsequently lose their faculty of becoming either masculine or feminine in type. In his recent excellent paper, Schiller (20) expressed the opinion that these tumors originate by reason of an error in differentiation of the mesenchymal core of the developing ovary. According to this explanation, the mesenchyme of the primitive gonad is undifferentiated when invaded by germinal cells from the primordial gut. Instead of normal development into Sertoli cells or granulosa cells of the normal testicle or ovary, the mesenchyme, by chromosomal malformation, may be transformed into neutral cells which remain as fetal remnants, later to develop into a sexually nonspecific neoplasm. In his classification, Schiller is able thus to place dysgerminomas in the group of ovarian tumors arising from tissue not normally found in the female gonad but present because of cellular malformation of the mesenchymal core into nonspecific interstitial tissue. Seegar's opinion that the histogenesis of dysgerminomas is not established is supported by Ewing's recent statement that "the embryology of the ovary is highly obscure."

Part of the increased interest in ovarian neoplasms stimulated by Meyer's work has been

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indicated by the re-examination by various investigators of old records and specimens in an effort to reclassify solid ovarian tumors according to the new terminology. Thus Meigs (11, 12) in studying histologically the ovarian tumors found at Massachusetts General Hospital between the years 1924–1935 discovered 5 cases of dysgerminoma; Russell found 7 such tumors after an examination of the specimens of 30 years at University College Hospital School (London); 3 cases were found in the Gynecological Museum of the Long Island College of Medicine by Wolfe and Kaminister; Seegar in 1938 collected 79 cases of dysgerminomas from the literature and added 19 more found among the pathological specimens at Johns Hopkins. In an analysis of 400 solid ovarian tumors removed surgically at the Mayo Clinic, Dockerty found 9 instances of dysgerminoma, or an incidence of 2.25 per cent; Klaften in a similar survey at Universitaets Frauenklinik in Vienna found an incidence of 3 per cent in 188 solid ovarian tumors. We have attempted a like investigation at Charity Hospital of Louisiana at New Orleans, covering the period 1932 to 1940, but among a group of 68 solid ovarian tumors found at operation and at autopsy, we have discovered only one dysgerminoma, that being the case which first initiated this study and which is herewith reported. Other results of our investigation will be reported in a subsequent communication.

CLINICAL CHARACTERISTICS

In the renaissance of interest in ovarian neoplasms an early observation was the high incidence of dysgerminomas among pseudohermaphrodites and in women with poorly developed genitalia. In the former group it is said to be the most common new-growth. The preponderance of pseudohermaphrodites in Meyer's series has already been alluded to. Of 64 cases reported by Fauvet, 27 were in pseudohermaphrodites and 2 were in true hermaphrodites. Of Seegar's collected series of 79 cases, only 50 were otherwise normal individuals, and of his 19 personal cases, 15 had normal external genitalia and secondary sex characteristics. Reported indications of low sexual potential in patients other than pseudohermaphrodites are such common symptoms as amenorrhea, delayed onset of menses, sterility, asthenia, oligomenorrhea, dysmenorrhea; the tumor with genital hypoplasia, infantilism, or with functionally inefficient gonads and breast hypoplasia occurs frequently.

It is generally agreed that dysgerminomas elaborate no specific hormone. The few biological assays which have been made have been inconclusively negative. Spielman and Morton reported the first study of extracts of the tumor for estrogenic and gonadotropic hormones and in this a weakly positive result was obtained for the latter hormone. Since an increase in gonadotropic or pituitary-like hormone has been observed repeatedly in amenorrheic females, no conclusions were drawn. These authors summarize the inconclusive results of the biological investigation of the urine by Wallis, Kleine, and Fauvet, and comment upon the paucity of data in this field. Seegar speaks of Zondek's assays of tumor and urine as also negative in result.

Although the consensus seems to be that the relation of dysgerminomas and female hypogonadism is coincidental and not causative, this conception by no means is universal. In writing of dysgerminoma, Meigs (12) states, "Its hormone is potent enough to prevent proper female development in some cases." Greenblatt and Pund hold much the same opinion. One of the Johns Hopkins cases was a female pseudohermaphrodite who, following the removal of a dysgerminoma from the left broad ligament, had a regression of male characteristics. A most interesting case is reported by Gough; that of a broad shouldered, muscular girl of 15 years who had a deep voice, male distribution of hair on body and face, and male habits. Following the removal of a large dysgerminoma there was a partial retrogression of these male attributes. Gough believes that in his patient the tumor elaborated abundant male hormone which inhibited the growth of the other ovary and caused the secondary male sex characteristics. He further suggests that in this group of patients normal female sexual development occurs only in those women in whom the tumor has arisen following the appearance of feminine characteristics.

A large pelvic tumor in a pseudohermaphrodite or in a female with infantile genitalia suggests dysgerminoma, but the diagnosis is not so easily made in those women who have normal secondary sex characteristics. Aside from symptoms referable to a disturbance of hormonal balance, the complaints and findings are usually those due to a large and rapidly growing pelvic tumor. Changes in the menstrual period, abdominal pain and enlargement are the common complaints. The tumor as a rule enlarges rapidly, attaining a size sufficient to fill the lower abdomen in 3 to 6 months. Degeneration of the fast growing mass frequently occurs and is sometimes responsible for fever, night sweats, and leucocytosis up to 20,000 cells per cubic millimeter. Other more infrequent symptoms, some of which are due to pressure, others to malignant extension, are renal colic, urinary frequency, respiratory embarrassment, diarrhea, vomiting, ascites, anemia, and loss of weight. The tumor is one of childhood and young adulthood, frequently having its onset early in puberty. Novak and Gray report its occurrence in a woman of 52 years, but more than 70 per cent of the tumors are said to appear before the age of 30 years (Dockerty and Seegar). In this characteristic it varies widely from its homologue, the testicular seminoma, which rarely is found before the thirtieth year.

The diagnosis rests largely upon a consideration of the duration of symptoms, the age of the patient, state of sexual development, and the presence of a rapidly growing pelvic neoplasm. Palpation of the abdomen and pelvic examination reveal a hard, elastic mass with an irregular, nodular surface. Occasionally the x-ray may be able to differentiate a teratoma or dermoid cyst from a dysgerminoma by demonstrating the presence of calcium in the tumor.

Opinions as to the incidence of malignancy in dysgerminomas vary all the way from that of Schiller (19, 20) in whose experience 70 to 90 per cent, and practically all unilateral tumors, were benign, to that of Wolfe and Kaminister and Greenblatt and Pund whose small series of 3 and 5 cases, respectively, all proved malignant. As yet there are such few cases on record and each writer's experience is so small that no clear conception of the degree of malignancy has been gained. The pathologist is able to add little to the problem's solution, for, histologically, all dysgerminomas display malignant features, and there appears to be no constant relation between these and the degree of malignancy. At present the most valuable criteria of the malignancy of individual tumors are clinical. If at operation a unilateral tumor is found which has no obvious extension, as indicated by the absence of infiltration of adjacent structures and regional lymph node involvement, it may be regarded as benign until proved otherwise by the clinical course. Infiltration of the broad ligament, uterus, opposite ovary, rectum and bladder, and lymphatic spread to the retroperitoneal lymph nodes occur in a definite proportion of cases, but metastases to distant organs are rare. Seegar was able to find only 2 such instances in the literature, one case in which there was metastatic involvement of the kidney and another case which spread to the liver; he added from his series one case of metastasis to the spleen, kidney, and pancreas. When extension has occurred there is a poor ultimate prognosis. However, the more efficient utilization of x-ray therapy may alter this situation since dysgerminomas seem to be affected by irradiation much like the lymphomas, being much more radiosensitive than the identical tumor in the testicle.

The importance of accuracy in estimating the degree of clinical malignancy at the time of operation is self-evident when the occurrence of dysgerminomas in young individuals is placed in relation to the effective methods of treatment of the malignant phase, viz., radical surgery and deep x-ray therapy. The price paid by the patient for this form of treatment is removal or destruction of both ovaries. While this fate is of little concern to the pseudohermaphrodite or to the patient with marked hypogonadism, it is greatly undesired by the young girl who has not yet developed secondary sex characteristics and by the young woman who desires to bear children. Seegar could find reported only 2 instances in which the opposite ovary showed neoplastic change after the removal of a dysgerminoma, but numerous reports are in the literature of

pregnancy ensuing following the operative removal of the tumor alone.

Simple extirpation has come to be considered good judgment on the part of the surgeon who finds at operation a solid, nonadherent, ovarian tumor. Should gross and histological study prove the mass to be a dysgerminoma, frequent follow-up examinations should be made in an effort to discover early any possible recurrence of the neoplasm, which when found should then be treated by irradiation. If, on the other hand, there is present at operation evidence of local extension, a more radical surgical procedure should be adopted and followed after operation by deep x-ray therapy. In inoperable cases, thorough irradiation alone remains the treatment of choice. Those patients whose advanced dysgerminomas are attacked early are offered an excellent prognosis.

PATHOLOGICAL CHARACTERISTICS

Dysgerminomas are bilateral in 20 to 35 per cent of cases (Dockerty and Schattenberg, 17, 18). They are usually comparatively large when seen by the pathologist, frequently being described as the "size of an adult head." The tumor mass is usually lobulated and frequently peculiarly kidney shaped. Over the smooth encapsulated surface run numerous dilated veins. Adhesions are essentially absent unless the capsule is perforated by malignant extension of the neoplasm, in which instance there may be an infiltration and adherence to any of the adjacent pelvic structures. The opposite gonad, normal or undeveloped, may be so completely replaced by tumor as to make sex determination impossible (Geist). The tumor is usually of a firm but elastic or doughy consistency.

The cut section presents a homogeneous, friable, glistening, brain-like surface through which run scanty fibrous septa. Areas of yellowish discoloration indicate lipoid degeneration, and frequently this has progressed to the stage of frank necrosis with the formation of broad zones of necrotic tissue and hemorrhagic cysts of varying size.

The microscopic appearance of sections of dysgerminoma is one of the most characteristic found among solid ovarian tumors. The tumor cells are large and round with hyperchromatic centrally placed nuclei containing large nucleoli, and a narrow lightly granular cytoplasm. Frequent mitotic figures appear. The cells are loosely arranged in columns or islands, frequently described as alveolar, separated by varying amounts of loose, edematous, poorly vascularized connective tissue. Degenerative changes and hemorrhages are common. The connective tissue nearly always is diffusely infiltrated with lymphocytes, and these with the presence of small epithelioid cells and large giant cells create a picture simulating tuberculosis. However, as Schiller (19, 20) points out, the giant cells do not lie in the center of the focus, as in tuberculosis, but often outside and even isolated between tumor cells. He suggests that there is a lipoid substance created by the necrosis of dysgerminoma cells which causes a tissue reaction similar to that stimulated by tuberculin. It would appear that much of the connective tissue in these sections is replacing areas of tumor necrosis and that the lymphocytic infiltration is a part of the same process. The entire histological picture is one of an undifferentiated, highly malignant neoplasm which closely approximates that found in seminoma of the testicle. A dysgerminoma in which there is scant stroma and in which the lymphocytic infiltration is not a prominent feature is easily confused with large round cell sarcoma.

CASE REPORT. A white man, of 21 years, was admitted to the Tulane Surgical Service of Charity Hospital on July 27, 1937, complaining of severe lower abdominal pain which had been present for 2 days. He had always been in good health and had never consulted a physician previously.

On close questioning he gave the following interesting history. From early childhood he had been shielded by his parents from the prying eyes of his brothers and sisters because of his abnormal external genitalia. He knew little about these except that his penis was small and that he urinated from a opening behind it. At the age of 13 there was a marked deepening of his voice and he began to have penile erections. He was always popular with the girls and went out a great deal with them. He stated that he had a "lot of passion" and that his penis remained erect for long periods of time after the slightest contact with a female. He found it necessary to shave once weekly. He had never menstruated.

Physical examination revealed him to be a slender young man of moderate height who was intelligent

Fig. 1, left. Photograph of the patient after operation, showing the size of the penis, the female distribution of hair, and the wide hips.

Fig. 2. Photograph of the patient showing a large glans penis, bifid scrotum, female urethral orifice behind which is the vaginal introitus.

and co-operative. The general impression which he gave was that of a boy several years younger than the stated age. He spoke in a low voice. The shoulders were narrow and the hips comparatively wide. The breasts were male in configuration, but there was a female distribution of pubic hair. The abdomen contained a firm mass filling the left lower quadrant, and in this same region there was marked tenderness and rigidity of the abdominal muscles.

The diameter of the penis was within normal limits, but there was a third degree hypospadias, and the penis was bound down by its frenulum so that it could not be lifted up in a position normally assumed during erection. Testicles could not be found. Instead of a scrotum there were present what appeared to be well defined labia majora. The urethral orifice was found between the bifid scrotum or labia at the base of the penis; just posterior to it was a vagina which appeared as a second opening, slightly larger, running internally to a small cervix uteri. On digital rectal examination, a small mass was palpated which was thought to be an infantile uterus; there was no evidence of a prostate. X-ray plates made after lipiodol injections of the vagina demonstrated a well formed canal which deviated to the right because of the left-sided tumor.

A clinical diagnosis of teratoma and hermaphroditism was made.

On August 7, 1937, laparotomy was performed by one of us. In the peritoneal cavity was a liter of xanthochromic fluid. A tumor the size of a large grapefruit was found protruding from the left side of the pelvis; it was twisted on its pedicle and some recent hemorrhage was observed beneath the capsule. This mass was apparently a neoplastic ovary. The opposite ovary was small, and the uterus and tubes were rudimentary. An unsuccessful search was made for testicles. After a bilateral salpingo-oophorectomy, the patient recovered in due course.

The pathologist reported that the tumor measured 19 by 11 by 8 centimeters. It was kidney-shaped, fairly firm in consistency, and had apparently an elongated, broad pedicle. The external surface was lobulated, and beneath the capsule could be seen several cystic areas. The opposite ovary measured 1 centimeter in diameter and was firm in consistency and white in color. On its surface was a small verrucous projection 2 millimeters in diameter. The attached fallopian tube measured 3 by 0.5 centimeters. The microscopic picture of the tumor was typically that of dysgerminoma. Sections of the opposite gonad showed that it too was the seat of similar neoplastic growth, in which were found small localized deposits of calcium. A nodule projecting from the

Fig. 3. Roentgenogram made after the vagina had been distended with iodinized oil. The vagina is pushed to the right by the large tumor.

Fig. 4. Drawing showing the large lobulated left ovarian tumor and the small right ovary and fallopian tube, with minute secondary neoplastic deposits on the surface of the ovary.

Fig. 5. Cut surface of the primary tumor, showing its lobular structure and areas of necrosis and hemorrhage.

surface of the smaller ovary consisted of tumor tissue in which there were many calcified areas.

The patient was readmitted on April 1, 1938, at which time there was no evidence of recurrence of the dysgerminoma. A first stage plastic operation was performed for the correction of the hypospadias. The patient was discharged with instructions to return in one month; however, he decided to retain his deformity rather than submit himself for further plastic procedures.

The patient was last seen on June 15, 1940, and at this time a thorough examination revealed no evidences of recurrence. He stated that he was in excellent health, had gained 20 pounds in weight since his operation, and was employed regularly. During the first 6 months following the removal of the tumor he had no penile erection; afterward, however, there were occasional morning occurrences. He was married 18 months before this interview, and although he has an erection and attempts sexual relations 3 or 4 times weekly, he has never been able to consummate intercourse because of the inability of the penis to assume a normal position during erection. On these occasions the penile engorgement gradually disappears after 30 or 45 minutes without a definite orgasm and without ejaculation. Neither is there discharge from the vaginal orifice at any time. This state of connubial frustration seems to be quite satisfactory to both parties, for the patient reiterated his complete marital happiness and firmly refused to undergo further plastic procedures.

Our patient has been called a female pseudohermaphrodite because we have been

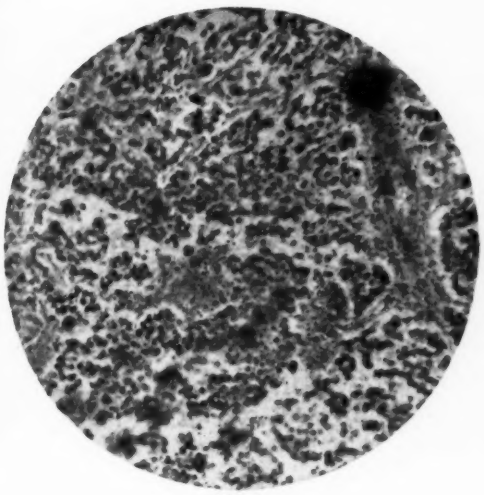

Fig. 6.

Fig. 7.

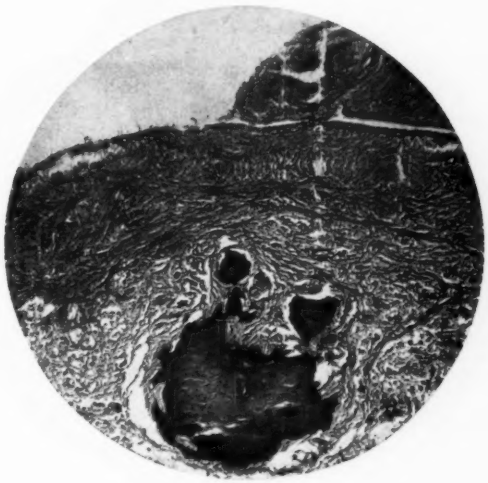

Fig. 8.

Fig. 6. Typical section of left ovarian tumor, composed of rather loosely arranged large round cells, with a scanty supporting stroma infiltrated by lymphocytes.

Fig. 7. High power view of section from left ovarian tumor showing more in detail the cells with their large hyperchromatic nuclei and the scanty supporting stroma infiltrated with lymphocytes. A tendency to formation of acini is evident.

Fig. 8. Low power view of section taken from right ovary, showing normal ovarian cortex beneath which lies neoplastic tissue surrounding a large deposit of calcium.

unable to demonstrate histologically both ovarian and testicular tissue and thus qualify him as a true hermaphrodite, a condition which Huggins, Cohen, and Harden could find reported in the literature only 15 times. The male characteristics can be explained by one of two assumptions: he may be a true hermaphrodite with testicles which we were unable to find; or this ovarian tumor may have elaborated the male sexual hormone. That the latter possibility may have been the case is suggested by the temporary diminution in sexual powers following the removal of the tumor, but is discredited by the subsequent development of a masculine sex urge.

SUMMARY

1. Dysgerminoma is a potentially malignant tumor which has its origin in the mesenchymal core of the ovary.

2. It occurs infrequently during the first three decades of life, most characteristically appearing in women with malformed or poorly developed genitalia.

3. Although generally considered without hormonal effect, it may have some inhibitory influence upon normal female physiology.

4. Gross pathological characteristics are its firm consistency, comparatively large size, and the homogeneous brain-like appearance of its cut surface. Microscopic sections show large round cells, which stand out distinctly, and scanty stroma infiltrated by lymphocytes.

5. Local extension is not uncommon, but metastasis to distant organs is rare.

6. Surgical removal, followed by irradiation in those cases with metastatic extension, is usually effective in the treatment of these tumors.

7. An example of this unusual tumor occurring in both ovaries of a pseudohermaphrodite is reported.

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USE OF SYNTHETIC, NONABSORBABLE SUTURE MATERIAL IN SURGERY

Preliminary Report

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DURING the past few years there has been a distinctly increased tendency to use nonabsorbable material for sutures and ligatures (1–4, 6–10, 13, 14, 16, 17). The time-honored catgut has its enemies but so does the silk, and the pendulum swings from time to time in opposite directions. To an impartial observer few points clearly stand out in the discussion of the relative value of both suture materials.

Catgut acts as a foreign body and in some individuals is apt to cause around the sutures a tissue reaction in form of an accumulation of serum with fibrin and leucocytic infiltration which, combined with the liquefaction produced in the disintegration and absorptive process of catgut, act as a fertile culture medium for bacteria. Moreover, some authors hold that catgut, a product derived from animal tissues, may be responsible for allergic reactions, although other writers consider the alleged antigenic properties of catgut a myth. Furthermore, there is uncertainty as to the time required for the absorption of catgut. Consensus is that catgut should not be used to suture the skin because suppuration invariably develops. Finally, the cost of catgut is relatively high.

On the other hand, the use of silk also has its limitations. The presence of infected wounds is considered by great many surgeons as a contraindication to the employment of silk, as sinuses may form. This statement is at variance with Meade and Ochsner's contention that the most important use of nonabsorbable sutures is in the grossly contaminated wounds, and with Shambaugh's claim (13, 14) that the presence of silk in suppurating wounds does not delay the healing process. Thompson agrees with Halsted that the presence of fine silk in suppurating wounds does not seriously impede healing. According to a prevailing opinion, silk should not be used for suturing the mucous membranes of the gall bladder and the urinary bladder because the sutures may act as nidi for calculi. Another disadvantage of silk is that it loses its strength from repeated sterilizations. The use of silk requires a meticulous technique including avoidance of tight sutures, mass ligatures, blunt dissection, etc. The fact that silk has established its reputation in thyroid surgery, repair of severed tendons and nerves, and other operations requiring a refined technique proves the great value of nonabsorbable suture material in surgery.

The value of cotton, linen, soft annealed steel alloy wire, and other nonabsorbable materials, is known but none of them has attained the popularity of silk and catgut. Inasmuch as the two last mentioned leading suture materials offer the aforementioned disadvantages, a search for good substitutes is justified.

Several years ago, while developing a new method for the preparation of so called corrosion specimens for anatomical studies, I was greatly impressed by the plasticity of a synthetic resin vinylite and it occurred to me that a derivative of this product, called vinyon, could be used as a suture material. Vinyon is a copolymer of vinyl chloride and vinyl acetate. The product lends itself to processing which permits manufacture of yarns with a wide range of tensile strengths and elastic properties. An ever increasing use is found for them in various branches of the textile industry. What facilitates the evaluation of vinyon in surgery is the fact that, unlike any other synthetic fiber, the tensile strength of the material is of the same magnitude in both the wet and dry stage. Furthermore, vinyon has a true elasticity comparable with that of silk, a unique property in synthetic fibers. The multifilament yarn is water-resistant, is not

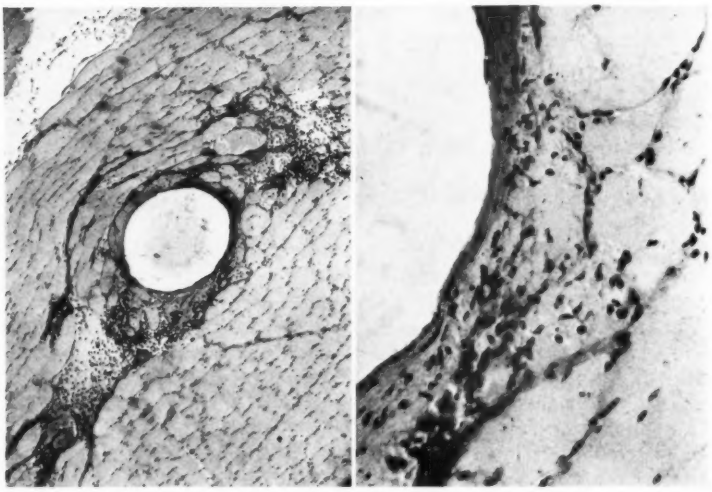

Fig. 1, left. Undyed zytor No. 0 implanted into a sacrospinal muscle of a rabbit. Specimen removed 3 days later. Low power magnification. Few degenerating muscle cells, very few polymorphonuclear leucocytes and a number of young fibroblasts.

Fig. 2. Same specimen, high power magnification. Several polymorphonuclear leucocytes; few muscle fibers degenerating due to the compression by the suture; several macrophages.

attacked by bacilli and fungi, and will not support such growth. Being thermoplastic, the product cannot be autoclaved for purposes of sterilization, but immersion in grain alcohol proved to meet all the requirements of asepsis.

On the present market vinyon is cheaper than silk. A cost comparison with linen is difficult because of the wide variation in sizes; however, in coarse sizes, 150 deniers and up, it is about the same or slightly cheaper than linen.

Another similar product, zytor, already on the market, was also tested as a possible substitute for silk. Vinyon is a polyvinyl resin; zytor, commercially known under the name "nylon," is a polyamide resin. Contrary to vinyon, zytor can be boiled or autoclaved and there is no serious effect of either procedure on the tensile strength of the material. After boiling 30 minutes in water, only 2 to 4 per cent and after autoclaving one-half hour at 15 pounds pressure, only 4 to 6 per cent of the original strength is lost. Braided zytor and braided silk are essentially alike in regard to tensile strengths. Zytor is made in two forms: multifilament and monofilament, and the first is braided.

What are the advantages of zytor over silk? Zytor sutures are less reactive in tissue than silk sutures. As far as the monofilament zytor is concerned, another advantage can be pointed out: here we have a noncapillary strand in which there can be no movement of tissue fluids along the strand and no nidation of bacteria. In the multifilament zytor, similar to braided silk, there are two forces of capillarity: (a) the water uptake of each individual fiber itself—in this respect zytor is superior to silk; (b) capillarity due to the small spaces between twisted or braided fibers; this capillarity is identical in both zytor and silk.

As to the relative value of both types of zytor, the multifilament type has the advantage in that knots hold better and the material is more pliable than the monofilament.

The manufacturer states that the price of the monofilament zytor compares with dermal sutures and the price of the multifilament zytor is approximately the same as that of silk.

Fanburg observed 4 cases of skin irritation in women wearing nylon hose. He suggests that the finish or the dye of the stockings rather than the yarn itself may be the cause

of dermatitis. Allergic reactions attributable to zytor suture material have not been observed by me.

To appraise the value of vinyon and zytor, the first mentioned suture material has been used in St. Elizabeth's Hospital in 30 unselected, consecutive clean cases requiring major surgery. In the following 30 cases vinyon was replaced by zytor. Both groups did not consist of an identical material but on the whole were formed by similar operations such as appendectomy, cholecystectomy, hysterectomy, oophorectomy, repair of postoperative hernias. The entire observation was confined to laparotomies. The synthetic suture materials have been employed for buried sutures of the peritoneum and fascia and also for skin closure. The gauge of both materials was an equivalent of catgut No. 000 and 0. Contrary to the customary advice not to use nonabsorbable material for continuous sutures, this mode was employed for closure of the peritoneum and the skin but the fascia was sutured with interrupted stitches. Vinyon or zytor respectively were also used for invagination of the appendiceal stump, approximation of broad ligaments after hysterectomies, ligation of the cystic duct, etc. In no case was there any evidence of irritation of tissues. At the end of 7 to 10 days, the abdominal wounds were completely healed and there were no signs of an inflammatory reaction. Vinyon or zytor and catgut were never employed together. Great attention was paid to the gentle handling of tissues, perfect hemostasis, clean dissection, avoidance of undue tension, and mass ligatures.

Although clinical impressions are notably unreliable, the theoretical considerations and the limited experience with the new suture materials show that they have sufficient merit to warrant further consideration.

SUMMARY

Two new synthetic suture materials, vinyon and zytor, have been studied on 60 unselected and consecutive cases requiring laparotomies. No essential differences could be established between vinyon and zytor. Both are very pliable, can be easily and repeatedly sterilized, do not fray, do not suffer impairment of their tensile strength in a wet stage, are not attacked by pathogenic micro-organisms, are nonirritating to the tissues, insusceptible to the action of tryptic enzymes, apparently nonallergic, and inexpensive. All these properties justify the prediction that the new suture materials will find acceptance in surgery as substitutes for silk and catgut.

Their main advantage over catgut is that of a nonabsorbable material in general, while the new products are superior to the silk (1) because they can be repeatedly sterilized by autoclaving or immersion in alcohol respectively without any untoward effect on their tensile strength, (2) the knots hold better, and (3) last, but not least, the tissue reaction is less pronounced.

Not enough emphasis can be laid on the necessity of a painstaking technique, with special attention to a meticulous care in gentle handling of tissues, perfect hemostasis and ligation of blood vessels without surrounding structures.

Further investigations are necessary to establish the value of these new suture materials in infected or contaminated wounds.

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THE LIGAMENTUM FLAVUM: ITS RELATIONSHIP TO LOW BACK PAIN

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THE problem of the varied and multiple causes of low back pain has for many years constituted one of the "great unknowns" of modern medicine, yet year by year a small part of this interesting jig-saw puzzle has been changed from the indefinite to the definite gradually but surely forming a part of a definite design which some day will be complete.

On embarking upon the research embodied in this paper we were of the opinion that if one small segment of discussion could be clarified a definite contribution would have been made. This was stimulated by the often repeated, but so rarely answered, simple interrogation "What constitutes the normal ligamentum flavum?" To the uninitiated this seems rather a far flung cry as a contribution to the etiology of a type of low back pain. However, the vast amount of proved cases of sciatic pain with demonstrable intraspinal pathology giving rise to pressure symptoms resulting either from changes of the ligamentum flavum, posterior protrusion of the intervertebral disc or both, has demonstrated the importance of the ligamentum flavum in the low back syndrome.

The structure was first noted to have pathological possibilities by Elsberg in 1913. It was not, however, until Towne and Reichert in 1931, showed that the ligamentum flavum might cause pressure upon nerve roots that its surgical significance was established. These authors attributed the condition to hypertrophy of the normal ligament, and this explanation was accepted by other investigators until recently. Attention was directed solely to size and relationship to the adjacent nerve roots as an explanation of its importance, and increase in size was assumed to be a simple hypertrophy of a normal structure. The question that crossed the minds of many has been: "Just what is the average normal and when may the ligament be said to be hypertrophied?"

It was this apparently simple question that caused Spurling and Rogers (11) first to attempt to establish by actual measurement what the "normal" size might be.

The ligament was also studied, measured, and described in comprehensive reports by Abbott in 1936 and 1938 (1, 2), Brown in 1937 and 1938 (3, 4), Naffziger and co-workers in 1938, and Horwitz in 1939.

Our objection to all this painstaking antecedent work is that the material was obtained from fixed cadavers and therefore did not establish a base line to which the normal and the abnormal could be compared, macroscopically and microscopically under *analogous conditions* to those found in the *living patient.*

The primary endeavor in our work therefore was to obtain fresh surgical specimens, to measure them under a standard technique, and to study them microscopically with standard methods of fixation and staining. This research was started in 1939, and while still in progress, Dockerty and Love from the Mayo Clinic in March, 1940, reported their results of measurements and microscopic findings in a series of 50 ligaments removed at operation for sciatica and backache.

Although, as we shall attempt to show, we do not attach much significance to the measurements given, our findings and conclusions from a histopathological standpoint strike a close parallelism.

As a result of this search for the "simple normal" it has been proved to our satisfaction that the so called "hypertrophy" of the ligamentum flavum does not represent an increase in size of the normal tissue, but rather a definite pathological change in the constituent elements of the tissue with a "substitution fibrosis" of varying degrees and amounts re-

From the Department of Surgery, Stanford University School of Medicine. Presented before the Western Orthopedic Association, San Francisco, September 7, 1940.

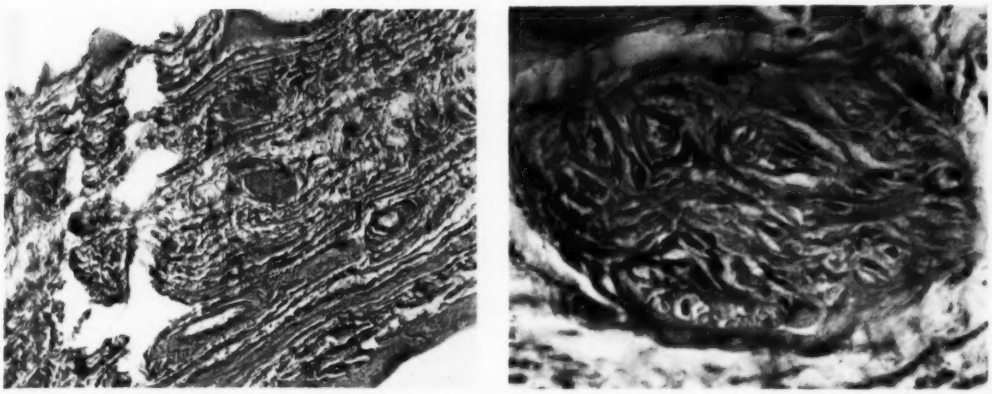

Fig. 1, a, left. Photomicrograph showing a nerve trunk or ending within a ligamentum flavum. The fibers are chiefly nonmedullated. ×65. b, The same under a magnification of 325 diameters.

placing the normal yellow elastic fibers, thus accounting for its change in size and appearance. We noted further that these pathological changes were not confined alone to that group of ligaments causing pressure phenomena and that similar pathology was apparent in specimens of ligamentum flavum removed for causes other than those producing intraspinal defects and nerve root pressure.

We soon found ourselves deviating from the realm of the concrete to the speculative as we attempted to correlate the clinical relief obtained in cases of kissing spine, localized trigger point pain in the lumbar region for which we had removed the ligamentum flavum and found the same histopathological changes.

The recent work of Steindler and Luck (12, 13) seemed to offer a logical explanation, if the pathological changes in the ligament were to be attributed as the etiological factor for this "posterior syndrome."

According to these authors, the nerve sinuvertebralis, which receives a white ramus from the common trunk and a gray ramus from the sympathetic chain just outside the intervertebral foramina and then turns back into the intervertebral canal supplying the neck and head of the rib, the pedicles, interior of the bodies of the vertebra, the loose areolar perimeningeal tissue and periosteum, was described about 1850, by Purkinje and von Luschka. They believe that reflex pain may be referable, on this basis, to lesions in and about the intervertebral canal and were able to break the reflex arc by injection of the localized "trigger points" with novocain.

In the type of case under discussion we, likewise, were able temporarily to alleviate the pain by a similar technique. No reference was made, however, to the innervation of the ligamentum flavum, and the question of its nerve supply, if any, demanded further investigation.

Reference to the literature revealed Spurling and Bradford (10) quoting some recent unpublished studies by Roofe, who found a profuse supply of sensory nerve endings in the annulus fibrosus and posterior longitudinal ligaments.

In this connection by special selective staining methods we have been able to demonstrate the presence of non-medullated nerve fibers in the ligamentum flavum, as illustrated in Figure 1. These findings substantiate the work of the previously mentioned investigators and specifically demonstrate a nerve supply to the yellow ligament. It might offer a logical explanation for the referred pain found in these cases and the reason for its alleviation by surgery.

BASIS OF PRESENT REPORT

We are reviewing 26 cases in which ligamenta flava were removed at operation, measured, and studied microscopically. These specimens were taken regardless of whether they

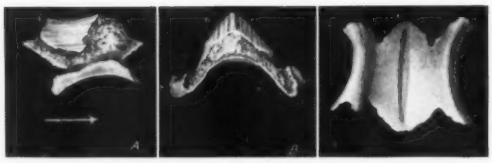

Fig. 2. Dissected specimen of ligamentum flavum from the level 4 to 5 lumbar. a, View from laterally; b, view from caudal margin; c, view as from within spinal canal.

were suspected of causing backache and whether they were related to a herniated intervertebral disc.

As a basis for microscopic comparison, cadaver specimens at various age groups, without known history of back trauma, were used.

Specimens studied were removed from cases of "congenital low back", vertebral disease, "kissing spine," "trigger-point" pain in posttraumatic low back disability without intraspinal protrusion. Microscopic sections were studied by differential staining methods, including hematoxylin and eosin, Mallory's connective tissue stain, Weigert's and van Giesen's. More than 400 sections were examined. It was found that selective stains for elastic fibers, especially the van Giesen, gave the most information.

FALLACIES OF MEASUREMENT

A brief survey of the anatomy of the ligamentum flavum will demonstrate the ease with which errors of measurement can be made. This structure is a saddle-shaped mass of connective tissue, light yellow in color and tough in consistency. It bridges the space between the laminæ, extending laterally to blend with the capsules of the lateral articulations, assuming its greatest thickness dorsally, mesially, and thinning out laterally in both directions.

It is apparent that, in order to obtain any standard of comparison, measurements must be made in analogous locations, as variations in thickness may be as high as a hundred per cent in the same specimen. Due to the elasticity of the structure, the degree of tension placed on the ligament is equally important. Our measurements were carried out with a micrometer with a constant bearing area and tension at a specified selected site. Fragments were discarded in which the planes could not be accurately orientated. It was found that specimens varied to such a degree with the size and development of the individual that no accurate generalization could be made as to the responsibility for symptoms from this factor. Moreover, of our two thickest specimens, both found in conjunction with herniation of a portion of the intervertebral cartilage in heavy, well developed young individuals, one specimen was normal histologically, according to our criteria, and one abnormal.

It is our conclusion, relative to macroscopic appearance, that the "normal" varies with the age, weight, physical development of the individual and the anatomical location of the ligament. Postural curves and spinal architectural deviations from the normal, with the presence of congenital anomalies, contribute to the variation.

It is not the size of the ligament alone, but the interrelationship of these factors, with or without pathological changes in the ligament that determines whether, in any particular case, the ligament is a causative factor for symptoms.

A typical example of the interrelationship of these factors (L. M., case 22 in series) was recently seen by one of us (M. C. M.). This patient had a moderate flexion injury to his lumbar spine one year previously followed by recurrent low lumbar backache with radiation of pain down one or both legs on effort. Although the pain was of sciatic type there were no sensory changes and no asymmetry of his reflexes. There was demonstrable roentgenologically a congenital anomaly of the articular facets of the third lumbar vertebra allowing the inferior articulations on both sides to be deviated toward the midline due to rotary changes in the isthmus.

Temporary relief only could be obtained by leg traction and a flexion plaster. Spinal puncture demonstrated a complete block below the level of the second lumbar and this was confirmed by air and lipiodol myelography.

At laminectomy a complete block was found due to the *combination* of the bony anomaly, a complete rupture of the third lumbar intervertebral disc, and the ligamentum flavum. It is certain that any of these factors taken sep-

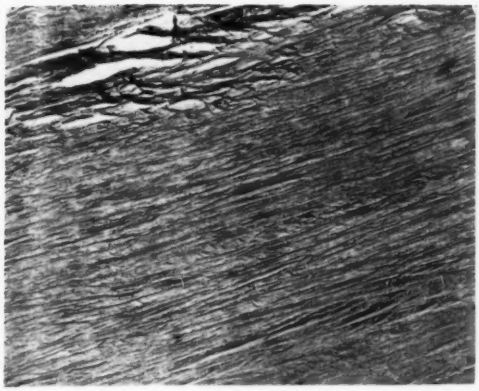

Fig. 3. Photomicrograph of *normal* ligamentum flavum. ×65. Note parallel laminations of elastic fibers in a fairly uniform wavy pattern, and relative absence of collagen elements.

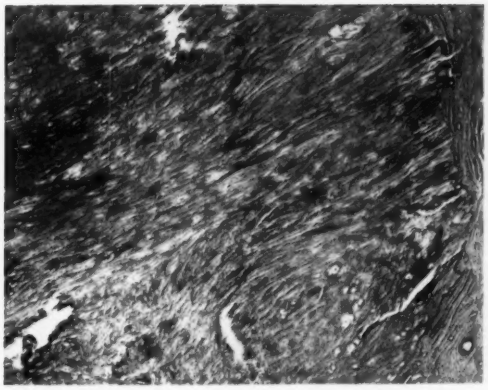

Fig. 4. Photomicrograph of ligamentum flavum showing *slight* fibrosis. ×65. Some regular clumps of laminated fibers still evident, but broken up and replaced in areas by collagen elements.

arately would not have given such a picture. This case is likewise unusual in having a rupture of the fourth intervertebral disc as well, all in the absence of obvious neurological findings.

HISTOPATHOLOGICAL FINDINGS

Histologically the ligamentum flavum is mesenchymal in origin, composed of specialized connective tissue. The three basic fibers of the connective tissue stroma are collagen, elastic and reticular fibers. The elastic fibers originate from a substance known as elastin, and give to the ligament its characteristic yellow color.

The normal ligamentum flavum consists of regular laminated bands of elastic fibers constituting an estimated three-fourths of the ligament. Collagen and ordinary adult connective tissue cells can be seen to make up about 30 to 50 per cent of the tissue volume. This is not seen, of course, in specimens stained selectively for elastic tissue; in fact, as one looks at such a preparation there would

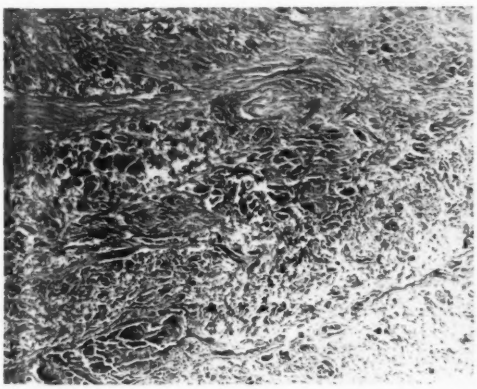

Fig. 5. Photomicrograph of ligamentum flavum showing *moderate* fibrosis. ×65. Note loss of regular pattern with predominance of collagen elements, and only small clumps of elastic fibers.

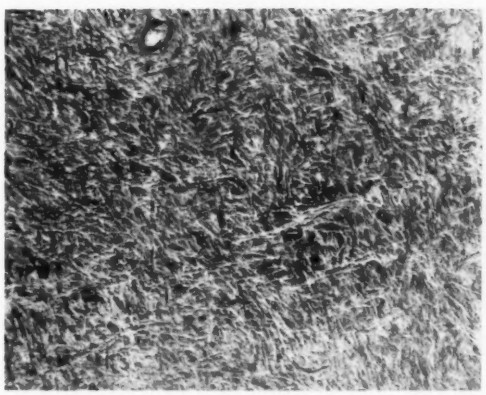

Fig. 6. Photomicrograph of ligamentum flavum showing *severe* fibrosis. ×65. Note absolute loss of definite pattern with only small, isolated elements of elastic tissue in a matrix of collagen substitution fibers.

seem to be little room for other tissue. When contiguous selections are otherwise stained, however, the relative importance of other connective tissue elements is apparent. Nor are the fibrocytes uniformly distributed through the sectioned ligament. They tend to be most prominent at the periphery (in all planes).

The yellow elastic fibers stream through the sections in broad, interlacing bands, interspersed in a definite wavy arrangement by collagen fibers through which an occasional blood vessel is seen. Fibrocytes are uncommon except at the margins of the ligament.

Toward the periphery of the normal ligament the orderly arrangement of the laminations is disrupted. The design is less compact, fibrocytes are more numerous, especially near the osseous attachment, some fatty tissue is present, and blood vessels are more in evidence. These blood vessels are thick walled.

The decision as to what is "normal" and what is "abnormal" among our specimens has been difficult. We have noted a variation in grade of abnormality from what we term a very slight fibrosis to marked fibrosis.

These abnormal findings are characterized by a progressive loss of the regular pattern with a break-up of the laminations of the elastic fibers and replacement in varying degrees by collagen fibers. The elastic fibers are sometimes fibrillated, broken in small clumps, or replaced by the collagen element. Gradations of change have occurred from slight disruption of the normal architecture to almost complete substitution by collagen.

ANALYSIS OF RELATIONSHIP OF PATHOLOGICAL LIGAMENT TO BACK PAIN

In cases with sciatica and evidence of nerve root irritation we have found no constant relationship between histopathological changes in the ligament and the symptom complex. Both in cases of proved dislocation of the intervertebral disc and those in which the ligament was felt to be the responsible factor, the microscopic findings have varied from normal to moderately advanced fibrosis. Indeed, in at least one case in which a normal ligament, microscopically, had been removed, there resulted a complete alleviation of symptoms. This leads us to reiterate, it is not necessarily the size or pathological changes in the ligament, but rather its relationship in the particular individual, that betokens its clinical importance in this type of case.

LIGAMENTS REMOVED FOR CAUSES OTHER THAN SCIATICA

In this series we found some of our most extensive fibrosis. In those cases in which a spinal fusion was performed, unfortunately, we shall be unable to determine what significance the demonstrable change in the ligamentum flavum might have had. However, the 3 cases in which the ligament was removed together with the interspinous ligament for "trigger point" pain, have resulted in complete alleviation of symptoms. We have previously speculated as to the relationship of these pathological changes in the yellow ligament to localized chronic back pain following trauma. As opportunities present themselves, we expect to make further observations upon this matter.

It seems prudent to call to the attention of other investigators that we believe that degenerative factors of age and use enter into the pathological picture of this structure as it does in other tissues. To illustrate this point, one of our series was a man of 65 years. In this case, sections showed replacement of the elastic fibers by collagen elements to the extent of about 90 per cent. In this patient surgery instituted for a demonstrable intraspinal block was not followed by relief of pain in the back.

CONCLUSIONS

1. Size and thickness of the ligamentum flavum alone are unimportant as possible etiological factors in back pain and sciatica, unless changed by trauma or disease, or causing pressure symptoms in combination with skeletal and/or nuclear changes.

2. Measurements are unreliable due to technical factors which prevent the establishment of any fixed standards. Size and thickness varies with age, anatomical and pathological structural changes, and location in the individual case.

3. The ligamentum flavum reacts to disease or trauma by the loss of the normal archi-

tecture of the elastic fibers and the development of a "substitution fibrosis" with replacement by collagen elements in varying degrees.

4. Definite degenerative factors occur in this structure with advancing age, giving similar pathological changes to those seen in trauma and disease.

5. The term "hypertrophy" is unsuitable as no increase in elastic elements with the preservation of the normal histological appearance has been observed.

6. A definite nerve supply—chiefly nonmedullated in type—to the ligamentum flavum has been demonstrated and presents a further anatomical explanation for certain aspects of "Steindler's posterior syndrome."

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THE MECHANISM OF URETERAL OBSTRUCTION IN PROLAPSE OF THE UTERUS

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IN 1847 Virchow was the first to call attention to the fact that complete prolapse of the uterus was frequently accompanied by hydroureter and hydronephrosis. Subsequently, Froerich, quoted by Brettauer and Rubin, reported a case of prolapse of the uterus with fingerwide dilatation of the ureters. He believed that the ureteral dilatation was due to a stasis in the bladder caused by a kinking of the urethra.

In 1907, Halban and Tandler carried out careful topographic studies on 23 cadavers with prolapse of the uterus. In 15 of these the ureters were dilated. They called attention to the fact that the entire ureter was dilated except the distal portion near the bladder. The dividing line between the dilated and undilated portion of the ureter corresponded with the edge of the levator muscle which forms the lateral border of the hiatus genitalis, or genital rupture ring through which the prolapse of the uterus and of the urinary bladder occurs. As a result of the descent of these organs through this ring, the ureter is pressed against the edge of the levator muscle and occluded by compression.

Brettauer and Rubin in 1923, following a careful review of the literature, felt that the mechanism of ureteral occlusion in prolapse of the uterus might be explained in one of the following ways: (1) kinking of the urethra and stasis in the cystocele (hourglass formation of the bladder); (2) intramural stretching in the bladder wall with stenosis; (3) compression of the ureters outside of the bladder. They also mentioned that the uterine artery might play a rôle in compressing the ureter.

Schmitz and Laibe in 1929 studied the changes in the upper urinary tract in prolapse of the uterus. They came to the conclusion that the hydroureter and hydronephrosis in procidentia are caused by a combined torsion, kinking, and edema of the ureter in its vesical portion.

Wallingford in 1939 suggested that the uterine artery in prolapse formed a sling over the ureter and produced a compression of the latter when the uterus descended.

Maher and Wosika in 1939 reported that prolapse of the uterus is frequently accompanied by a hypertension. In 97 cases of procidentia studied by them, hypertension occurred in 74, or 76 per cent. They ascribed the hypertension to hydronephrotic changes in the kidneys and stated that "while the exact mechanism of ureteral compression does not seem entirely clear, obstruction is consistent with complete prolapse." In fact these authors in making their intravenous urograms used the compression effect of pulling the prolapsed uterus downward instead of the conventional abdominal compression.

From these studies it is clear that although numerous theories have been advanced as to the manner in which the ureters may become occluded in procidentia, proof of the exact mechanism has not heretofore been given. It is, therefore, the purpose of this paper to present a new mechanism and to demonstrate it upon the living subject by roentgenographic means.

In order to appreciate the manner in which the ureter may become occluded it is necessary to review the fundamental topography of the ureter in the female pelvis. From its origin at the ureteropelvic juncture the abdominal ureter courses downward in back of the posterior parietal peritoneum, to which it is more or less loosely attached. As it dips down into the pelvis over the linea innominata, it crosses the external iliac vessels. It then courses downward, forward, and medially through the broad ligament, lateral to and at a varying distance

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Fig. 1. Second degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. The left ureter shows an acute downward angulation.

Fig. 2. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep downward angulation of the left catheter which has also been pulled down out of the upper ureter.

from the cervix uteri. After a short interval it enters the wall of the urinary bladder.

The course of the abdominal ureter is best observed through the routine lumbar kidney incision. As the parietal peritoneum is stripped forward from the posterior abdominal wall, the ureter, which is loosely attached to the peritoneum, moves forward with it.

The pelvic ureter, however, is best approached through a laparotomy for the purpose of topographic study. As it crosses over the external iliac vessels in descending into the pelvis, it is covered only by the pelvic peritoneum. It is freely movable at this point and is easily located by palpating the pulsation in the iliac artery. If the overlying peritoneum is then incised, thus exposing the artery for a short distance, the ureter will be seen crossing it. The ureter may then be lifted out of its bed and dissected free in a downward direction, with ease, until the broad ligament, in which the ureter lies firmly imbedded, is reached. During its course through the broad ligament the uterine artery crosses above the ureter—occasionally it may cross below it.

It, therefore, becomes evident that the ureter has three fixed points of attachment: (1) at its origin from the renal pelvis, (2) during its course through the broad ligament, and (3) at its entrance into the wall of the urinary bladder. Elsewhere it is more or less freely movable. Whereas a huge retroperitoneal or renal tumor may dislocate the upper ureter even beyond the midline without causing an appreciable ureteral compression, a tubo-ovarian abscess which points into the broad ligament or an intraligamentary fibroid may cause serious ureteral obstruction.

The broad ligament, in which the ureter lies so firmly imbedded, also plays an important rôle in supporting the uterus under normal conditions. Mengert in 1936 carried out a very careful study on the cadaver to determine the exact structures which support the uterus, and how impairment of these structures leads to procidentia. He placed each cadaver on its back on a table in a horizontal position. With the aid of tenaculum, a cord was attached to the cervix and carried over a pulley at the foot of the table, where a 1 kilogram weight was

Fig. 3. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep downward angulation of the left ureter. The apex of the kink descends down through the pelvic outlet.

fastened to the cord. In this manner a horizontal pull of 1 kilogram was exerted on the cervix. He then opened the abdomen and divided various structures adjacent to the uterus. When the infundibulopelvic ligaments, the round ligaments, and the upper third of the broad ligaments were divided, no descent of the uterus occurred. But when he divided the lower two thirds of the broad ligaments, considerable descent followed. When the paravaginal tissues on both sides were divided, complete prolapse was accomplished. The supporting structures according to Mengert are fibrous tissues which extend laterally in a broad band from the lateral aspect of the cervix and lower portion of the corpus, to attach to the fascias at the pelvic brim. A similar band of fibrous tissue likewise extends laterally from either side of the vagina to the brim of the pelvis. The fibrous tissues in the lower part of the broad ligament have also been described as a dense band which is known as Mackenrodt's ligament.

In summarizing these findings it is seen that a dense band of fibrous tissue lies in the lower two thirds of the broad ligament between its peritoneal coverings. This band extends laterally from the cervix and lower portion of the corpus to the pelvic brim. The ureter in its course through the broad ligament lies firmly imbedded in this portion of the broad ligament.

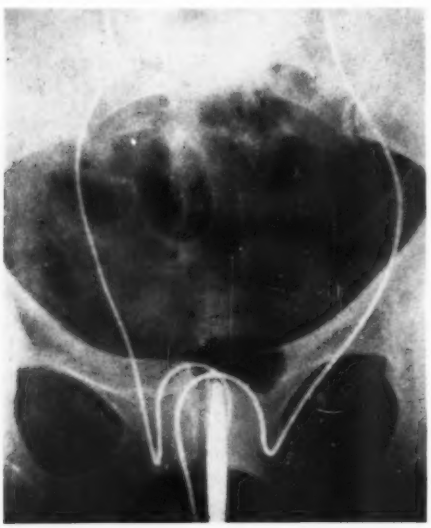

Fig. 4. Third degree prolapse of uterus. Roentgenogram with ureter catheters in place, uterus pulled downward. Note acute, shallow, downward angulation of both ureters.

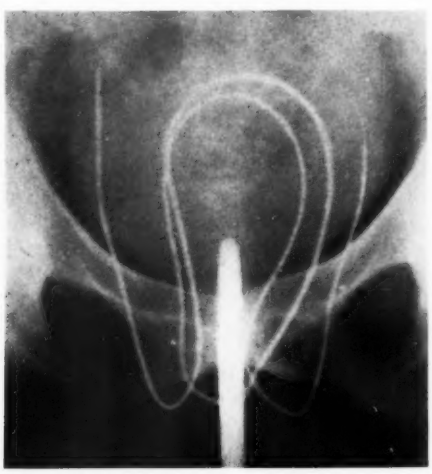

Fig. 5. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep, sweeping, downward looping of both ureters which have descended out of the pelvis. The catheters have been pulled down out of the upper ureters by this descent.

It is, therefore, our opinion that when prolapse of the uterus occurs, the broad ligament, with its contained fibrous tissues, forms a sling which pulls the ureter downward and produces a kinking as well as a compression of the latter. If this is the case, this mechanism should be readily demonstrable in procidentia on the living subject by roentgenographic means.

Ten patients with prolapse of the uterus were selected for this study. Roentgenographic studies of the ureters were carried out with the uterus in the normal position and after it had been pulled down with a tenaculum attached to the cervix. At first an attempt was made to demonstrate the lower ureter by intravenous urography and then by retrograde pyeloureterography; but both of these methods proved unsatisfactory because the lower ureter failed to show when the uterus was pulled downward, probably because the dye was driven away from this region by the kinking and stretching of the ureters.[1]

It was, therefore, decided to delineate the course of the ureters by inserting thin, soft, radio-opaque catheters to the renal pelves and to take roentgenograms with the uterus in the normal position, and after it had been pulled downward. At first anteroposterior, lateral, and oblique views were taken. But since it soon became evident that the anteroposterior exposure best showed the changes in the course of the ureter, and since the additional views did not give any further information, we decided to confine ourselves to the former.

As was to be expected, when the uterus was pulled downward, the changes in the ureters varied from a short, acute, downward kink to a wide, sweeping downward curve, which carried the ureter down out of the pelvic outlet. In fact, in one case this downward sweep was so pronounced that the tips of the catheters were pulled down in the ureters for a considerable distance. These changes were most pronounced in the cases of complete prolapse, and they were either unilateral or bilateral. Occasionally they were absent. Such an absence of the kinking of the ureter on one or both sides may be explained in the following manner: The very disintegration and relaxation of the fibrous bands in the broad ligament which contribute to prolapse of the uterus may have progressed to such an extent that these structures are no longer sufficiently intact to form a sling over the ureter when the uterus descends. More specifically the findings when the uterus was pulled down in the 10 cases studied were:

In 3 cases of first degree prolapse: 2 cases showed no alteration in the course of the ureter; in 1 there was a short, acute, downward angulation of the left ureter.

In 3 cases of second degree prolapse: there was no alteration in the course of the ureters in 1 case; the lower ureters descended (by stretching) but no angulation was seen in 1 case; there was a slight downward angulation of the left ureter in 1 case (Fig. 1).

In 4 cases of the third degree prolapse: there was an acute deep downward angulation of the left ureter in 2 cases, which was so deep in 1 instance that the apex of the kink descended out of the pelvis (Figs. 2 and 3); in 1 case there was a shallow, sharp, downward angulation of both ureters (Fig. 4); in 1 case there was a deep, sweeping downward looping of both ureters which descended well out of the pelvis. As a result, the ureter catheters were pulled down out of the upper ureters (Fig. 5).

[1]This undoubtedly explains why the exact mechanism of ureteral obstruc ion in uterine prolapse has not been demonstrated previously in any of hundreds of roentgenographic studies which have undoubtedly been made in such cases in the past.

SUMMARY

1. It has long been known that complete prolapse of the uterus is frequently accompanied by ureteral obstruction, which may lead to a dilatation of the ureters and renal pelves.

2. Although numerous theories have been offered as to the manner in which this obstruction is produced, the exact mechanism has not previously been demonstrated.

3. On the basis of topographic anatomical studies, a new mechanism is suggested. The broad ligament with its contained fibrous bands, which are attached laterally to the fascias at the pelvic brim and medially to the cervix and corpus uteri, forms a sling over the ureter and pulls it downward when the uterus descends. This produces a marked downward kinking of the ureter.

4. This downward kinking of the ureter is readily demonstrable on the living subject by radiographic means.

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INTUSSUSCEPTION IN ADULTS

A Consideration of Therapeutic Measures and a Case Report

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INTUSSUSCEPTION is preponderantly an affliction of infancy and early childhood with 75 per cent of the cases occurring in individuals under 2 years of age (21, 30); the disorder is relatively uncommon among adults but it is always critical and may afflict an individual of any age.

The intussusception of infancy is usually idiopathic, and while in adults it may likewise be idiopathic it usually, about 70 per cent of the cases (30), is associated with the presence of a tumor, a diverticulum, or an ulcer. In a group of 300 adult cases of intussusception analyzed by Eliot and Corscaden, one-third was due to tumors of which 60 per cent were benign. Martin and Love report intussusception following trauma and state that 4 other such cases have been recorded. A number of cases involving the sites of gastric and intestinal anastomoses have also been reported (7, 10), as have several instances of primary intussusception of the appendix (29).

Christopher stated in 1936 that, since Eliot and Corscaden's paper of 1911, 43 cases of adult intussusception due to benign tumors and 16 cases due to malignant tumors had been reported. These consist of the following varieties: of the benign group there were lipoma, 11 cases; adenoma, 9 cases; fibroma, 9 cases; polypi, 5 cases; papilloma, 2 cases; myxoma, 2 cases; leiomyoma, 1 case; carcinoid tumor, 1 case; enterocystoma, 1 case; adenoma of accessory pancreases, 2 cases: of the malignant group there were carcinoma, 10 cases; and sarcoma, 6 cases.

Christopher also stated that "twenty-five cases of intussusception in adults have been reported in which no tumor was found or at least described." He added one more case to this group and also one case to the tumor group. In the 3 years since his paper somewhat over two hundred reports concerning adult intussusception have been published in the world literature. Excluding those associated with concurrent abnormalities, only 14 idiopathic adult cases have been presented in the English literature during this period (4, 5, 6, 11, 15, 25, 32, 33). In this group 3 were proved by examination after resection and 1 was proved by postmortem examination; all the others were carefully inspected and palpated for evidence of causative pathology and none was found. The present paper describes an additional case belonging to the idiopathic group. This case occurred in the author's practice, and an account of it is presented in the appended report.

Intussusception of the gastrointestinal tract may occur at any point between the stomach and the rectum. Inasmuch as tumors are more common in the large bowel it is not surprising to find that the latter is more often the site of involvement in adults than is any other portion of the gastrointestinal tract.

The direction of the intussusception is nearly always descending. Lockhart-Mum-

mery states that, "retrograde intussusceptions do occur but only during death or as a result of asphyxia; they are not met in practice." Rosenblum writes, "ascending or retrograde intussusception occurs, probably, only just before death or at the time of death." Nevertheless, several such cases occurring during life have been reported in the last four years (9, 12, 15, 19). Moreover, a number of retrograde intussusceptions involving anastomoses have been recorded (7).

TREATMENT

Intussusception is a form of strangulation obstruction, the therapeutic approach to which involves the following considerations: (a) reduction, thereby relieving the obstruction and the circulatory impairment; (b) evaluation and disposition of the involved segment of bowel; (c) correction of possible etiological factors.

In common with other forms of strangulation obstruction, early diagnosis and treatment are prerequisites to successful treatment, though it is agreed that subacute and chronic cases may occur, and that, occasionally, a case may recover spontaneously by self-reduction or by sloughing the gangrenous segment and establishing an autoanastomosis. In contrast to other forms of bowel strangulation it is to be noted that this form may occur without localized tenderness or muscle spasm owing to the fact that the strangulated segment, the intussusceptum, is ensheathed by the intussuscipiens which thereby protects the parietal peritoneum from irritation. Appreciation of this fact is of importance and especially so in the early diagnosis of the disease.

Reduction. Two methods of reduction may be considered: (1) indirect manipulation by administration of enemas, and (2) manipulation through an abdominal incision. The former method is applicable only in instances of colocolic and ileocecal intussusception as it consists in an attempt to force back the intussusceptum by building up a head of pressure against it through the administration of air or fluid enemas. Besides being limited in application this type of treatment is redundant with potential dangers and is more appropriately applied in the treatment of the condition in infants and children. Indeed, the really enthusiastic proponents of this form of treatment seem to have attained their success in the infancy and childhood age groups. Hipsley, whose report is notable, has demonstrated that it is a meritorious therapeutic measure in skilled hands. He states that he has successfully reduced 65 of 100 consecutive cases with a mortality of only 5 per cent for the entire group. Admirable as these results are, it should be realized that not many surgeons have had extensive experience in treating such cases, and consequently are not in a position to acquire the proficiency of judgment which will permit them to recognize readily the cases of incomplete reduction. Furthermore, in infants and children the intussusception is usually uncomplicated by other pathological conditions, whereas in adults the reverse is true and operative procedures are commonly necessary to eradicate the causative pathological process. Obviously, hydrostatic treatment does not permit the removal of a tumor or a diverticulum nor does it permit recognition of nonviable bowel. Injudiciously applied hydrostatic pressure may cause perforation of the bowel if exerted against a devitalized bowel wall, and especially so in one involved by tumor.

Retrograde intussusceptions, though rare, do occur and usually are not recognized preoperatively. In these instances the administration of enemas would certainly be contraindicated. Moreover, a seriously sick patient who may ultimately have to come to operation would not be improved as a surgical risk if treated previously by colonic distention.

The use of barium enemas under fluoroscopic control as a diagnostic aid, on the other hand, is often indicated for it enables one to ascertain the position of the lesion and it may even identify the intussusception. An abdominal roentgen film without the administration of contrast media, can and should be taken in all suspected cases, for, as recently pointed out by Schatzki, the roentgenological diagnosis of intussusception can often be made on the basis of this alone.

Manipulation through an abdominal incision. The first maneuver which is usually employed in manual reduction is the application of

manual pressure over the apex of the intussusceptum with coincident light traction on the proximal free bowel. It is essential that such a procedure should be executed with gentleness for overzealous efforts may result in tearing the bowel or mesentery which, because of edema and impairment of circulation, is abnormally susceptible to the trauma of traction. Frequently an appreciable degree of edema is present in the proximal portion of the intussusception and may cause sufficient constriction to make withdrawal of the intussusceptum difficult or impossible. One may attempt to overcome such a condition by compressing the mass at the point of constriction, thereby squeezing out some of the edema fluid into the adjacent tissues. Sometimes it is possible to insert a finger gradually between the intussuscipiens and intussusceptum and dilate the neck of the passage; in addition, a finger tip so introduced may be hooked into the wall of the intussusceptum, thus permitting light traction distal to the constricted point. In the case reported in this paper the intussusceptum was spirally twisted and reduction was accomplished only after a finger had been inserted as above described and manipulated in a manner partially to unwind the spiral formation; approximately 2 inches could be unwound at once and this portion was then easily withdrawn, following which further unwinding and withdrawal was possible. By these alternate manipulations reduction of about 12 inches of bowel was accomplished and then the remainder of the invaginated loop was easily withdrawn.

Management of irreducible intussusception. Occasionally the neck of the invagination is so tight that the above manipulations are ineffective and under these conditions it may be incised with scissors just as one performs a dorsal slit for phimosis. This procedure is advocated by Brown. It will frequently release the incarcerated segment which may then be drawn out. The incision is best made on the antimesenteric side of the bowel, and following reduction the incision is closed by a double row of sutures.

The Jesset operation has also been advised for the treatment of irreducible intussusception (28). This operation consists of incising the intussuscipiens and from within its lumen amputating the intussusceptum as high as possible. An operation of this character may permit the correction of the deformity but exposes the patient to the danger of peritonitis as it requires a large incision in the bowel wall and involves a considerable amount of manipulation by instruments and hands in contact with intestinal mucosa. Contamination of the peritoneum under such conditions is almost unavoidable. Consequently, the operation must be regarded as likely to be unsatisfactory and fraught with danger.

A very satisfactory procedure to which one may resort is fixation of the intussusception *in situ* with interrupted sutures about its neck and sidetracking it by means of a lateral anastomosis, the success of which depends upon the relief of the obstruction, and also upon the protection of the peritoneum by the viable wall of the intussuscipiens. Frequently the intussusceptum sloughs off and is passed spontaneously through the rectum. The following reports exemplify the rationale of such treatment.

Kingsford reported the case of a 46 year old man in which, owing to the critical condition of the patient, he limited the operative procedure to a lateral anastomosis between the ileum and transverse colon. Six days later 18 inches of necrotic bowel was passed by rectum. The patient recovered. Montgomery and Mussil reported 2 similar cases in infants. Recovery followed, though no slough was passed.

Bockoven, Thompson, and Mayo have each reported cases in which the diagnosis was missed, no operation was performed, and spontaneous recovery was accompanied by the passage of the sloughed bowel segment.

Pryde reported the spontaneous passage of 6 inches of intussuscepted small bowel in a postpartum patient who was discharged apparently well 14 days later. However, 2 weeks later the patient was operated on because of a recurrence of symptoms. An obstruction due to inflammatory reaction at the site of the auto-anastomosis was found. Resection and end-to-end anastomosis was then done, and the patient recovered. This case is illustrative of the wisdom of the advice of Eliot and Corscaden.

These authors reivewed 43 cases in which the necrotic bowel passed spontaneously per rectum; in some of the cases lateral anastomosis alone had been performed and in the remainder no operation had been done. They concluded that, "in cases cured by sloughing although temporary relief is usually afforded by nature's method, yet within 18 months, and usually much earlier, secondary obstruction develops from cicatricial contraction at the point of the original invagination, and is rapidly fatal. Such an unfortunate termination appears so common that after the subsidence of the abdominal symptoms associated with the discharge of the slough in these neglected cases, the writer suggests the advisability of providing against the contingency of subsequent obstruction by establishing a lateral anastomosis between the intestinal canal on either side of the invagination."

This opinion is well substantiated by the experimental work of Montgomery and Mussil, who created artificial intussusception in 25 dogs. In 11 of the dogs they also created a short circuiting anastomosis. The 11 dogs with the anastomoses lived and remained well, but when killed and examined 60 days later they all presented cicatricial contractures at the site of the sloughed invagination. Of the 14 dogs without anastomoses 2 died from hemorrhage 2 days after operation, 2 died from acute obstruction within 5 days, 1 showed no evidence of obstruction either antemortem or postmortem, and 9 dogs lived an average of 34 days before dying of chronic bowel obstruction.

From this evidence it may be deduced that an irreducible intussusception can be safely left within the abdomen provided the immediate obstruction is relieved and the eventual cicatricial stenosis at the site of the sloughed invagination is provided for. This may be done by a short circuiting anastomosis or, in certain poor risk cases, by a colostomy or ileostomy as a first stage procedure with subsequent short circuiting or resection of the stenosed area of colon. Such a solution to a difficult problem has a great deal of appeal, for it is an acceptable method whereby the surgeon may shunt an acutely ill patient around the dangers of a resection. It is especially valuable when dealing with infants and children in whom resection is so often fatal.

Management of prolapsed sigmoidal intussusception. The fact that some sigmoidal intussusceptions prolapse through the anus renders them unique and makes possible a special operative approach to the problem of disposal of the affected bowel. The method to be used is similar to that employed in the rubber band treatment of rectal prolapse as advocated by Reid. Wangensteen (31) and Bayard each reported a case successfully treated by the application of a rubber band in such a manner that the prolapsed sigmoidal intussusception sloughed off at its neck.

The technique used in these cases in general was as follows: Under spinal anesthesia with the patient in a steep Trendelenburg position, a firm rubber tube approximately 1 inch in diameter was passed through the lumen of the invaginated and prolapsed sigmoid to a level several inches beyond the point of involvement; a tight rubber band was then slipped up over the invaginated sigmoid to the level of origin of the invagination. The intussuscepted sigmoid eventually sloughed off due to the constriction of the bowel wall between the rubber band and rubber tube and an autoanastomosis was established. In Bayard's case the band was placed about 5 inches above the level of the anus, and the slough came away on the ninth day. Wangensteen reported separation of the slough on the fifteenth day and noted that it occurred at a point about 1 inch above the level of the constriction. Bayard's case was symptom-free 1 year later and at that time showed no evidence of stricture of the rectum. If stricture should develop following this type of operation, it would be fortunately at a point amenable to dilatation. It has been suggested by Wangensteen that gas gangrene antitoxin be given prophylactically in such cases.

The above procedure appears to offer a rather simple method whereby intra-abdominal resection may be avoided in patients with sigmoidal intussusception with prolapse, which are irreducible or nonviable, or both. It is essential that the surgeon be able to reach the neck of the invagination and he must be certain that no loops of small bowel have become

insinuated between its walls if the manipulation described is to be carried out with complete safety. Laparotomy might well complement this operation, for by it, one could better evaluate the magnitude of the lesion, locate more accurately the point for constriction, and be assured that no loops of small bowel are involved in the process.

Resection. If resection becomes imperative because of coexisting pathological process, the surgeon must decide whether a one stage or two stage procedure is indicated. In fact, the principles governing bowel resection in general should be closely adhered to.

Prophylactic measures. If reduction has been accomplished and examination of the gut shows no presenting pathological condition, there remains only the consideration of the means of preventing recurrence. In ileocecal involvement, the surgeon may perform a cecopexy or may suture a short section of ileum to the lateral wall of the cecum in an attempt to effect a mooring of the bowel. Bayard, in a paper dealing with intussusception of the sigmoid, which he states is the most common site of chronic intussusception, describes the following procedures for the prevention of recurrences: (a) plication of an excessively redundant mesentery; (b) suture of the longitudinal striae to the psoas fascia; (c) elevation of the pelvic peritoneal floor and obliteration of the pouch of Douglas by placing fascia lata strips across and beneath the peritoneum and attaching them to the pelvic brim on either side. These measures may be worth-while if no tumor is present. If, however, tumor is present, which is usually the case in this region, resection or exteriorization with secondary closure will be necessary and this will be sufficient to prevent recurrence. Some surgeons feel that preventive measures should not be attempted (28).

CASE REPORT

On December 16, 1939, H. F., a 28 year old male, was admitted to the Haverhill Municipal Hospital with a history of having had dull, cramp-like, periumbilical pain off and on for the preceding 11 months. During the preceding month he had had daily nausea and pain which would awaken him every morning and this pain would frequently last all day. At times the pain consisted of a constant dull ache and the patient said he never felt completely free from it. The past history was not significant except that appendectomy had been performed 14 years previously.

On the day of admission to the hospital, the patient was awakened at six o'clock in the morning with severe, constant, periumbilical pain which became progressively worse, and was accompanied by nausea and vomiting. Physical examination revealed nothing of significance with the exception of marked tenderness in the right side of the abdomen, most prominent in the mid-third, and a definite mass in the same region lateral to the old appendectomy scar. There was a moderate degree of spasm present throughout the right side of the abdomen. Peristaltic sounds were not heard on auscultation. The mouth temperature was 97.4 degrees F. The pulse rate was 80. The blood pressure reading was 110/60. The white blood cell count was 21,800. A diagnosis was made of strangulation obstruction, involving the lower ileum, probably due to adhesions.

Laparotomy revealed a large mass involving the cecum and ascending colon as far as the hepatic flexure. The cecum was edematous and contained an intussusception of the ileum. An attempted reduction was made by applying manual pressure over the apex of the intussusception while gentle traction was exerted on the proximal ileum. This procedure was of no avail. A finger was then inserted at the neck of the invagination in such a manner as to dilate it sufficiently so that a finger could be passed along the side of the intussusceptum. When this was done it was found that the intussusceptum was spirally twisted. Alternate maneuvers of unwinding and applying traction led to the reduction of the intussusception which proved to be of the ileocolic type. Approximately 3 feet of ileum were involved in the process. This segment of ileum was dilated, pale, and moderately edematous. Careful palpation of this section of bowel revealed no tumors, diverticula, or other conditions which might have been responsible for the occurrence of the process. A few adhesions were found between the cecum and the parietal peritoneum and also between the uninvolved ileum and the peritoneum, but none of these adhesions appeared to play any part in the etiology of the condition. The ileum was replaced in the abdominal cavity and no further operative procedures were attempted.

The patient made a normal convalescence and was discharged from the hospital on December 30, 1939, feeling well.

In the 14 months which have elapsed since the operation he has had no symptoms referable to the intestinal tract.

SUMMARY

Varieties of adult intussusception are reviewed, and various therapeutic procedures are discussed. A case of adult intussusception which was apparently idiopathic is presented.

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THE TERMINAL COMMON BILE DUCT AND DUODENAL PAPILLA

A Roentgenological Consideration

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IN the routine roentgenological study of the duodenum, many anatomical changes occur in the ampullary segment. Although these changes seemingly are of scant importance, they are of inestimable value in the diagnosis of pathological conditions. The literature pertaining to roentgenology and textbooks on the use of the roentgen-ray in gastrointestinal disease pay scant attention to the interior of the descending duodenum, and very little is mentioned regarding the roentgenological criteria of affections involving the terminal common bile duct and the duodenal papilla. There seems to be a lack of knowledge regarding the roentgenological manifestations of disease of this segment of the bowel, which no doubt accounts for the paucity of information.

Recent roentgen-ray investigations of the interior of the digestive tract have contributed considerable information regarding the earlier manifestations of pathological conditions. A study of the roentgenological appearance of the normal interior of the ampullary portion of the duodenum has been presented in a previous communication (1), is of invaluable aid in determining the presence of disease in this segment. Although minimal changes occurring in this portion of the duodenum often challenge the acumen and vigilance of the roentgenologist, a discussion of these changes will no doubt lead to a better understanding and improvement in the diagnosis of diseases affecting this portion of the bowel. As a result of the confusion and lack of knowledge of the roentgen-ray picture produced by the various diseased processes involving this region, minimal or early changes in the mucosa and the contour of the duodenum have been given little consideration. The necessity for a roentgenological investigation of the ampullary segment of the duodenum has therefore become increasingly important, due to the fact that the majority of cases of disease of the terminal common bile duct and papilla are either misinterpreted or not recognized. However, a re-study of roentgenograms of many proved cases of disease of this segment has shown that there were distinct, demonstrable, minimal changes which were not recognized at the time of the roentgen-ray examination. Failure to recognize abnormalities in the ampullary portion of the duodenum is in part due to lack of knowledge of the roentgen-ray criteria of diseases demonstrable in the interior of the duodenum.

The descending portion of the duodenum is of especial interest because of its relation with the terminal common bile duct, the papilla, and the head of the pancreas. It must be strongly emphasized that lesions involving the terminal common bile duct or the duodenal papilla invariably affect the duodenum, either by invasion of the lesion or by producing a pressure defect upon the configuration of the mucosa or its exterior contour.

In this communication the normal roentgen-ray appearance of the interior of the ampullary portion of the duodenum will be briefly discussed, and the anatomical changes occurring in the mucosa, papilla, and terminal common bile duct considered. The roentgenological picture of the duodenum is ordinarily a relief of the interior. Normally the transit of the barium meal caudad through the duodenum is very rapid, but it is rarely empty as long as the barium is being expelled from the stomach. Some barium nearly always remains in the duodenum long enough to obtain a view of its interior and contour. Serial roentgenograms, presenting views in different stages of filling and emptying of the duodenum are essential for the proper investigation of the ampullary portion. By the utilization of the fluoroscope, large gross lesions can easily be detected. Changes in the mucosal folds, the demonstration of the papilla and other minute findings are best observed in serial roentgenograms, preferably without compression, although at times compression is useful in delineating the pathological process. The normal mucosa of the interior of the descending duodenum is portrayed by transverse circular folds known as Kerkring's folds. These folds project into the lumen, consist

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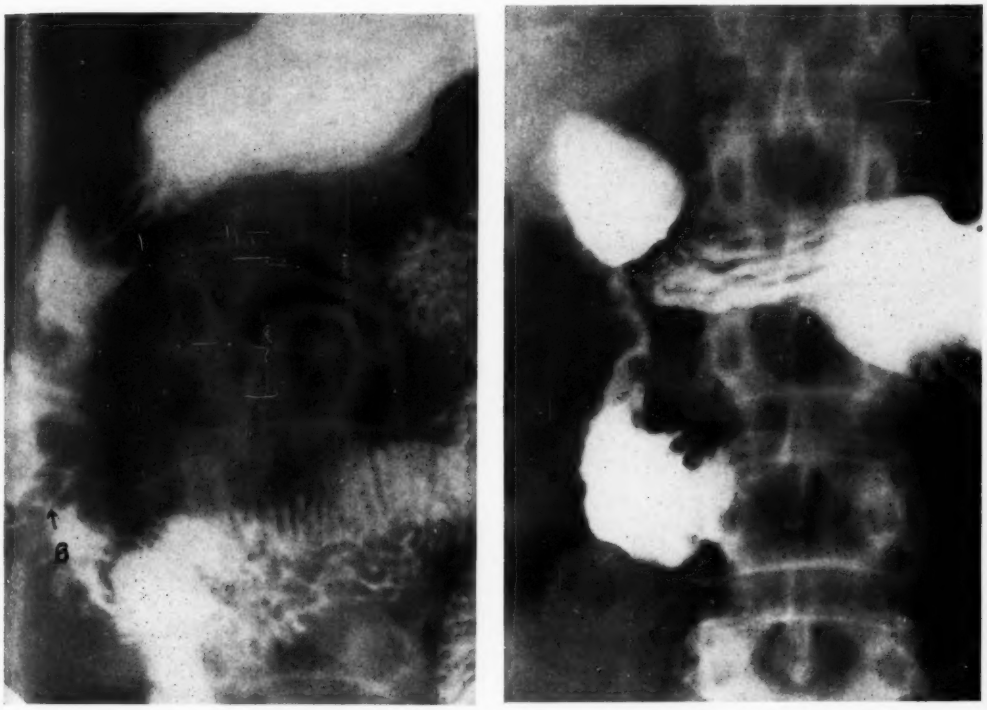

Fig. 1. a, left, A pressure defect in form of an inverted three is shown on the inner aspect of the ampullary portion of the duodenum at arrow *A*. Slight enlargement of the duodenal papilla is shown at arrow *B*. Right, A narrowing of the lumen of the duodenum, with obliteration of the transverse folds. There is also some evidence of pressure on the inner aspect of the duodenum, due to a duodenitis with secondary changes in the head of the pancreas.

not only of the mucosa but also of a supporting submucosa and do not disappear under compression.

The ampullary portion of the duodenum at the juncture of the posterior and left wall reveals a slight elevation projecting into the lumen, which is produced by the traversing common bile duct. Over this area is seen a low longitudinal fold known as the plicae longitudinalis duodeni. This fold is interrupted by the duodenal papilla, but continues below the papilla for a short distance. The latter fold normally varies from 4 to 6 centimeters in length and from 2 to 4 millimeters in width. At its beginning it is shallow, but becomes more prominent as it approaches the papilla. Roentgenographically it produces a single longitudinal narrow negative shadow. Occasionally this fold may be demonstrated in the normal subject; however, it is more often portrayed in affections involving the terminal common bile duct. In the early stages of disease of the common bile duct, this fold becomes enlarged, thickened, broadened and more prominent, and produces more or less characteristic mucosal changes in the interior of the duodenum. In later stages, changes in the contour of the duodenum, as well as varying degrees of stenosis, are often demonstrated.

The bile papilla or major duodenal papilla projects into the lumen as a prominent nipple-like process, through which the biliary and pancreatic ducts usually empty. The roentgenological demonstration of the normal major duodenal papilla has likewise received little attention. The papilla can be demonstrated in many instances in the mucosal relief view of the interior of the duodenum. The normal papilla roentgenologically presents itself as a small rounded, more or less circular negative shadow, varying from 3 to 5 millimeters in diameter. It has the appearance of a punched out hole. Occasionally a hood-like semicircular fold may be seen atop the papilla.

Fig. 2a.

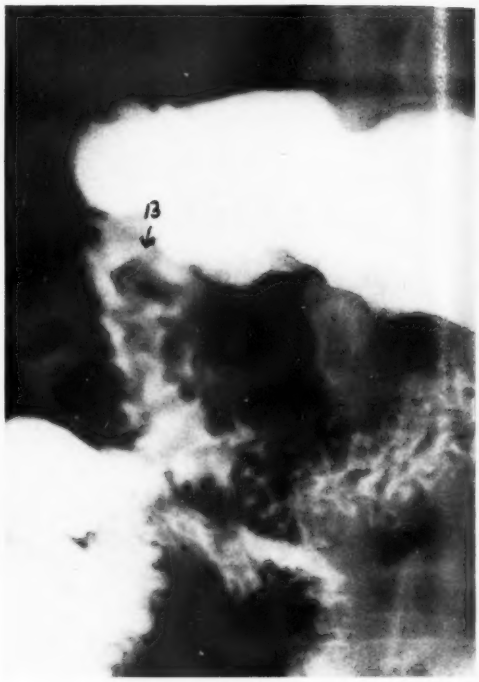

Fig. 2b.

Fig. 2. a, A punched out defect is shown at arrow *B*, in the upper descending duodenum in region of the minor papilla. A broad longitudinal fold is observed extending below this defect. There is some compression of the inner aspect of the ampullary portion of the duodenum, due to pancreatic pressure. Note the ragged appearance of the contour of this segment. b, Same case. A large negative shadow is demonstrated at arrow *B* similar to the defect in the opposite roentgenogram. The defect simulates a polyp, but since it is continuous with the longitudinal fold it is probably an enlarged minor papilla. Contour of descending duodenum is ragged due to inflammatory changes.

Close inspection of the mucosal contour of the papillary area may at times reveal minute changes that are indicative of early pathology. Any enlargement of the size of the papilla must be carefully studied for early pathological manifestations. The enlargement varies according to the stage of the disease. In late cases it may become large enough to produce changes in contour of the duodenum and varying degrees of stenosis.

Anatomical changes produced by inflammatory affections cause swelling in the ampullary area, papilla, and terminal common bile duct. Benign and malignant tumors will produce changes which are chiefly manifested in the wall of the duodenum, causing definite contour change as well as changes in the configuration of the mucosa. Although clinical and roentgenological data are often deemed to be adequate to sustain the diagnosis of a pathological condition, the similarity of roentgen-ray findings frequently makes results difficult to interpret accurately. A histological roentgen-ray diagnosis cannot always be made with certainty. However, since the most conspicuously affected portion of the duodenum is isolated to a small segment surrounding the papilla, careful clinical and roentgenological studies will often lead to a correct diagnosis. It has frequently been stated that lesions of the terminal common bile duct and papilla cannot be diagnosed by means of the roentgen ray. However, one should correct this impression, for it is believed that a large percentage of cases can be correctly diagnosed when attention has been focused upon this segment of the duodenum. Numerous isolated proved cases of pathological affections of the terminal common bile duct, have been gathered from the literature to corroborate the roentgenological criteria which are established in this presentation. The roentgenological data are further strengthened by the numerous autopsy

Fig. 2c.

Fig. 2d.

Fig. 2. c, Narrowing of the duodenum is illustrated in the same case and also compression from the head of the pancreas is shown at arrow *A*. d, Same case, oblique view, narrowing of the lumen of the duodenum is shown at arrow *A*. The longitudinal fold is not seen in this position, except at arrow *B*, where a short longitudinal fold is seen below the region of the major papilla. An ulcer niche defect is shown in the duodenal bulb at arrow *C*.

and surgical observations. Impressive cases of carcinoma of the common bile duct have been described in the more recent literature and have revealed roentgenological changes that are more or less diagnostic. Notwithstanding the fact that it is often stated in the literature that the routine gastrointestinal roentgen-ray examination yields little information regarding pathological changes in the terminal common bile duct, the failure to diagnose such cases cannot be charged altogether to roentgenography, but rather to a lack of experience and knowledge of the roentgenological criteria produced by diseases affecting the ampullary segment of the duodenum. Since the terminal common bile duct and papilla are closely related to the duodenum, and since most lesions involving them encroach upon the lumen, they must in some way produce anatomical changes which should be recognized by means of the roentgen-ray. When lesions ulcerate or when stenosis occurs the pathological change should be quite characteristic. It must be borne in mind, however, that at times it is very difficult to evaluate slight departures from the normal.

The following roentgenological signs may be observed in affections of the terminal common bile duct and the major duodenal papilla: (1) enlargement and broadening of the plicae longitudinalis duodeni fold, (2) encroachment of the enlarged duodenal fold upon the lumen of the duodenum, (3) mucosal changes surrounding the longitudinal fold and changes in the pattern of the ampullary mucosa, (4) enlargement of the major duodenal papilla, (5) filling defect in the contour of the duodenum, (6) varying degrees of stenosis, (7) secondary ulceration producing a defect, (8) invasion of the pancreas which may produce signs of pancreatic pressure on the contour of the duodenum, (9) cholecystographic changes, producing nonfilling of the gall bladder when the bile duct is occluded, (10) pressure defect of the stomach in late cases.

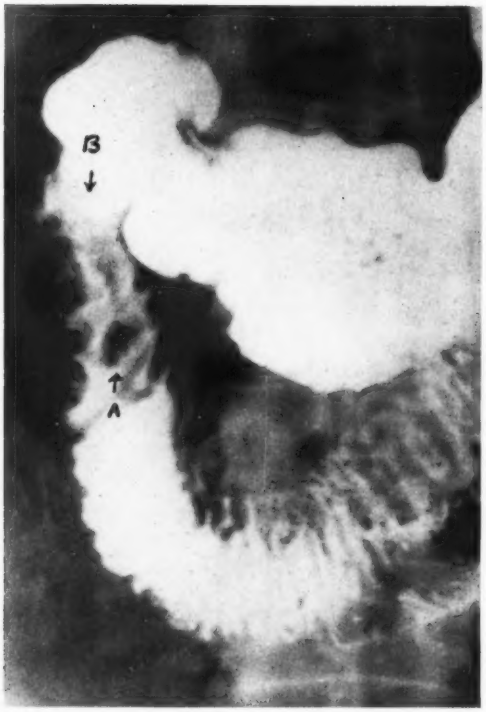

Fig. 3. Roentgenogram illustrating a wide longitudinal fold at arrow *B*. An enlarged papillary negative shadow is shown at arrow *A*. Note the ragged contour of the upper portion of the descending duodenum, due to inflammatory changes.

Inflammatory conditions of the terminal common bile duct roentgenologically present a thickened, broadened plicae longitudinalis fold and also enlargement of the papilla. The transverse folds are shortened as a result of the projecting swollen longitudinal fold into the lumen. There are often secondary inflammatory changes involving the duodenum, producing a characteristic picture of a duodenitis, with narrowing of the lumen, and changes in the mucosal picture of the duodenum.

In carcinoma of the terminal common bile duct and papilla, the fold is enlarged in varying degrees, according to the stage of the disease. In the early stages the findings are similar to those caused by an inflammatory process, but in later stages the fold becomes quite large, prominent, and persistent, and produces a marked encroachment upon the lumen with a filling defect in the contour of the duodenum. There are also changes in the mucosal pattern denoting a neoplastic lesion. The papilla frequently becomes enlarged, producing a filling defect of an intraluminal duodenal lesion. The defects resulting from the enlargement of the longitudinal fold and that of the papilla are portrayed roentgenographically as negative or translucent areas displacing the barium. The caliber of the lumen is narrowed in varying degrees. In lesions involving the common bile duct alone, the defect is usually smooth and sharply outlined. When the duodenal wall is invaded the defect is quite irregular. Lesions involving the papilla produce a defect simulating a polyp. The defect is usually smooth, but in later stages it becomes irregular as the duodenal wall is invaded. Stenosis of the duodenum is usually a late manifestation and frequently indicates duodenal invasion. The degree of stenosis varies, but it is rarely complete. In benign obstructive lesions there may be some dilatation proximal to the lesion, while in malignant conditions the lumen reveals no dilatation. In late stages, especially in carcinoma, it may be very difficult to differentiate a primary duodenal lesion from that of a primary common bile duct or papillary lesion.

In benign tumors of the papilla, the size of the papillary defect is considerably increased, depending upon the size of the tumor. Roentgenologically the lesion is depicted as a smooth, rounded enlargement in the papillary area producing a large sized negative defect, simulating a large hole.

Stones in the terminal common bile duct cannot as a rule be demonstrated in the relief roentgenograms of the interior of the duodenum, unless the stones contain an excess of calcium.

Ulceration when present can be shown at times surrounding the common bile duct area, by the crater produced. Recognition is difficult, since its crater is often shallow; but changes in the mucosal pattern may give a clue to this condition.

The mucosal pattern of the interior of the duodenum invariably shows some demonstrable changes in its configuration. In neoplastic diseases the mucosa is either obliterated or displaced in the affected area. The break in contour of the normal transverse folds is readily shown in serial roentgenograms. Large lesions are ordinarily seen under the fluoroscope. As the plicae longitudinalis duodeni fold becomes enlarged, the transverse folds are displaced laterally, so that in the roentgenograms the transverse folds are not continuous folds, but seem to end abruptly at the enlargement. A similar picture is seen in the region of the papilla, where the transverse folds may be shown to be displaced and obliterated by the encroaching tumor mass.

Fig. 4. a, left, Anteroposterior view is shown of a proved case of carcinoma of the terminal common bile duct, demonstrating an annular defect. b, Same case, oblique view.

The irregular contour of the duodenum and also the slightly widened longitudinal fold are shown at arrow *A*. (Case of Dr. Samuel Brown, Cincinnati.)

Tumors originating in the duodenal wall, roentgenologically simulate those occurring in the papilla. However, tumors originating within the terminal common bile duct have several characteristics by which they can be differentiated from those of the duodenum, especially in the early stages of the disease. Malignant tumors of the duodenum are more often an infiltrating or a polypoid lesion which originates in the interior of the duodenum. These are more apt to produce an irregular filling defect and cause stenosis much sooner than those originating in the duct. Those occurring in the duct produce early biliary symptoms, while those occurring primarily in the duodenum produce secondary gastric disturbances in the early stage, and when biliary symptoms occur, these are late manifestations. In the later stages of disease involving the common bile duct and the papilla, when the duodenum has been invaded, it is then difficult for the roentgenologist to determine the exact origin of the tumor. This also holds true for the surgeon, when exploration is made.

In carcinoma of the terminal common bile duct, the contour of the external duodenal curve is not affected and there is no displacement of the duodenum. The defect is often sharply outlined. The plicae longitudinalis duodeni fold is enlarged, and thickened. The major duodenal papilla may also be enlarged. The mucosal pattern is distorted and the mucosa is displaced. There is frequently some degree of encroachment upon the lumen; although it is very slight in the early stages of the disease, it may become very marked in late instances, when there may be varying degrees of stenosis. When stenosis occurs the defect is annular and smooth, but is often irregular in later stages. Occasionally ulceration or secondary changes in the pancreas may be observed.

The effect of lesions of the terminal common bile duct and papilla upon the pancreas is roentgenographically less striking. Not infrequently however, the pancreas is invaded in cases of carcinoma or there may be some swelling of the head of the pancreas secondary to duodenal affections which produce characteristic roentgen-ray changes in the contour of the duodenum. This is evidenced by the slight pressure upon the inner aspect of the ampullary portion of the duodenum, producing an inverted three defect (2).

The effect of lesions of the terminal common bile duct and papilla upon the cholecystographic study of the gall bladder is quite obvious. There is frequently a nonfilling of the gall bladder, though there may not be any actual anatomical disturbance of this organ. The gall bladder may be faintly visible on the flat film in some instances as a result of an empyema following biliary obstruction. A normal gall bladder may be dilated and visible on the plain roentgenogram. In some cases in which the obstruction is incomplete, the dilated gall bladder becomes visible following the administration of dye. The association of gall stones in cases of terminal common bile duct pathology occurs less frequently than in cases of other biliary diseases.

In affections of the upper common bile duct, proximal to its entrance into the duodenum, there may be evidence of pressure upon the adjacent structures, such as caused by carcinoma, or dilatation of the common bile duct due to other conditions. It may produce a pressure defect upon the duodenal bulb or superior duodenum, or upper portion of descending duodenum. In rare instances in the presence of a duodenal diverticulum, a pressure defect may be seen in the diverticulum.

The clinical features of intrinsic obstruction of the common bile duct are almost indistinguishable from those produced by extrinsic pressure, such as from carcinoma of the head of the pancreas. There are, however, several clinical differences which should be considered. In the case of intrinsic bile duct obstruction, there are few constitutional symptoms at the onset. There is usually pain following the sudden onset of obstruction. The symptoms simulate those of common duct stones. On the other hand, obstructions due to extrinsic pressure are usually painless. Of especial interest is the fact that lesions involving the terminal common bile duct and duodenal papilla give rise to symptoms very early in the course of the disease. Jaundice usually occurs at an early period and is the predominant objective sign. The clinical diagnosis of biliary obstruction is usually quite obvious, but the exact site and the nature of the pathological process is difficult to determine. However, a complete and thorough roentgen-ray investigation of the gastrointestinal tract and gall bladder may disclose the site and often the etiological condition. In obstructions of the common bile duct, there is usually a dilatation of the common bile duct and gall bladder, with enlargement of the liver as a result of biliary stasis.

SUMMARY

Minimal roentgenological changes in the contour and mucosal pattern of the ampullary portion of the duodenum are shown to represent pathological conditions. Many pathological affections involving the terminal common bile duct and major duodenal papilla are often overlooked in the early stages. Occasionally some abnormality is recognized but is often difficult to interpret because of lack of knowledge of the early roentgen-ray manifestations of disease that occurs in this portion of the duodenum. Roentgenographical changes in the ampullary segment are emphasized as a point of origin for the majority of lesions occurring in the duodenum, exclusive of the duodenal bulb. The roentgen-ray investigation offers the best means to diagnose correctly affections of this portion of the duodenum. A number of facts stand out pre-eminently in this study, namely:

1. The basic roentgen-ray criteria of the normal interior of the ampullary portion of the duodenum are reviewed.

2. Changes in the normal mucosal pattern are discussed.

3. The roentgenographical criteria of pathology of affections of the common bile duct and major duodenal papilla are described.

4. Diseases involving the terminal common bile duct and papilla invariably produce some changes in the duodenum.

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FERRULE CAPS FOR THE HEAD OF THE RADIUS

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CERTAIN fractures of the head of the radius may lead to surgical removal of the head if there is resulting distortion of the rounded articular surface from fragmentation and comminution, especially when there is displacement of fragments, some of which may penetrate through the joint capsule completely. Necessity for this operation may also arise in the complications after fracture of the ulna or dislocation of the radius or of both bones at the elbow. Delayed causes leading to desire to remove the head may be found in excessive new bone formation about the head and into the elbow joint or surrounding tissues ending in loss of pronation and supination or interference with full flexion and extension of the forearm, partial or complete bony ankylosis of the elbow joint, painful joint containing loose or attached osseous bodies, or interference with the radial nerve from local pressure or callus inclusion.

The necessity for removal of the head of the radius develops most frequently in adults—very seldom, if ever, in children. Some of the delayed causes may be traced to too early active or passive movement of the elbow joint and a failure to immobilize fractures considered to be lacking in sufficient osseous damage to warrant primary excision of the head of the radius. In the course of healing after fracture, during a convalescence of permitted movement, no immobilizing splint having been employed, new fibrous tissue and new bone easily overdevelop, which process may terminate in shrinking of capsular capacity, fixation to surrounding structures, ankylosis of the joint in part or completely, and setting up of severe pain with dysfunction. Such results often follow a failure to comprehend the nicety of the rotatory mechanism supplied by the superior radioulnar articulation and its basic importance in the acts of pronation and supination of the forearm. In the adult, this close-fitting rotating joint will not tolerate much irregularity on its articular surface without functional impairment. Consequently, resection of the radial head and neck proximal to a point where it becomes extra-articular may avoid many complications within the joint leading to impaired function. All operations described in this article have followed my continued practice of limiting the procedure within the joint, not cutting the orbicular ligament nor injuring the radial nerve. To accomplish this the resection must be accompanied by gentle removal of all osseocartilaginous fragments, whether loose or attached, by a straight cutting off of the neck without leaving projecting bone spicules, and by a minimal amount of irritation and damage of the synovial surface and of any part of the surrounding joint structures. For many years also I have advocated closing over the resected open neck of the radius with pieces of periosteum, or nearby soft parts of transplanted fascia. On the other hand, much of the limitation of elbow joint motion after these injuries can be traced to periarticular fibrosis and thickening of the capsular structures set up by the tearing and hemorrhage of the primary injury or subsequent irritation from unwisely forced movements in the presence of distorted bone fragments.

Following simple removal of the head and closing of the joint, the forearm may be flexed in full supination to approximately 80 degrees with the arm and held there by a suitable plaster-of-Paris splint from the base of the fingers to the axillary margin which immobilizes the joint and precludes any rotation of the forearm. Such a splint must be worn until the hemorrhage into the joint and surrounding tissues, the combined result of fracture and operation to remove the head, has been absorbed. Motion after a too early freeing from splint support may merely lead to an increased restriction of function. This splintage may last as long as 6 to 10 weeks. Thereafter, as healing is controlled by x-ray examination in an endeavor to eliminate the possibility of new bone formation, application of local heat and active use short of pain may be helpful in curtailing convalescence and hastening functional return.

The cut-off neck may then round out and cause no local joint restriction, or it may perversely lead to local new bone and fibrous tissue formation and restriction of joint motion. In addition to these local changes, the loss of the head and part of the neck of the radius after removal may affect the distal radioulnar joint by permitting the radius to foreshorten in its longitudinal axis in spite of the support of the interosseous ligament between the two forearm bones. This possibility may follow

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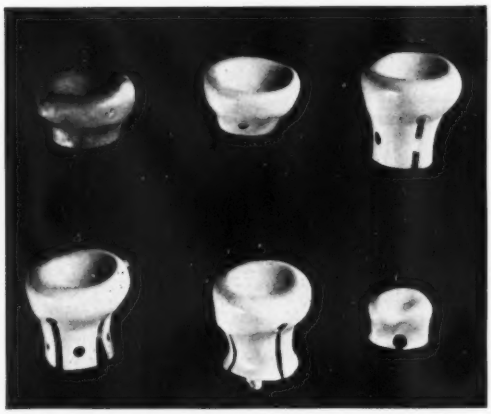

Fig. 1. Evolutional series of vitallium caps used for replacement after resection of head of radius. *1*, Resected normal head of human radius. *2*, First type of ferrule cap with small holes for suture or nail insertion to fix onto shaft. *3* and *4*, Caps with longer and slit skirts, permitting adjustment at time of operation for purpose of slipping over neck of radius. *5*, Final type of cap used with center pin, which can be inserted into medullary canal of bone (Fig. 2). *6*, Cap used for experimental work on dogs, the final model with center pin not shown here.

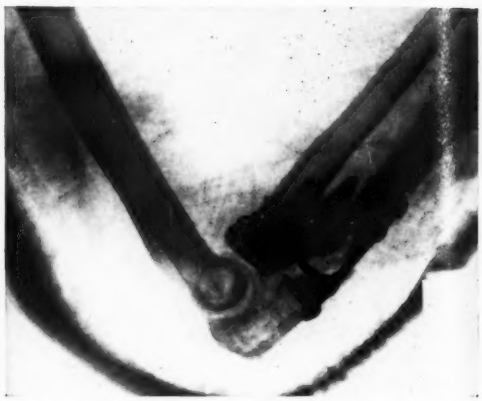

Fig. 2. Postoperative film showing ferrule cap with center pin placed accurately on the neck of the radius with sufficient space between it and the condyle of the humerus. The small vitallium plate holding the ulna has failed to grasp the intermediate fragment completely, but alinement is satisfactory. This went on finally to bony union and about 50 per cent recovery of full function.

when the ligaments at the wrist have been in some measure disrupted at the time of the original injury without full clinical evidence of fracture or dislocation of the head of the ulna or even looseness of the distal radioulnar joint, because the surgeon overlooked this in considering the all too evident damage of the structures in the elbow joint. Shortening of the length of the radius may disarrange the distal radioulnar joint, upset the normal relationship of the two styloid processes at the wrist, and bring the normally more distal radial styloid back to the horizontal level of the ulnar styloid or further, when viewed in the roentgenogram. The patient's honest efforts to increase the range of rotatory motion at the elbow may add to this derangement by increasing vicarious function and irritation of the distal radioulnar joint, ending in painful wrist, lack of power, and some radial flexion of the hand with changed external appearance, characterized by undue prominence of the head of the ulna. Therefore, the more nearly an anatomically accurate filling in of the hiatus following removal of the head of the radius is obtained by any means, the more content the surgeon may feel that an important factor in the avoidance of undesirable after-results following this mutilating but sometimes necessary procedure may result. This factor is a close second in importance to the nicety of the resection of the head without stripping of periosteum of the diaphysis, without spattering bone fragments and cells potentially osteogenetic into the joint or the periarticular tissues. This includes the squaring off of the end of the shaft fragment without splintering. The third important factor in treatment is rest in a supporting splint and sling for 4 to 6 weeks to permit quiet healing without new bone formation. The vitallium cap may overcome some or all of these difficulties.

A tentative attempt to overcome some of these disabling changes has been made by the use of vitallium caps or ferrules, which may be fitted down over the cut-off neck of the radius at the time of removal of the head or even at a later stage, when new bone formation or restriction of joint movement has occurred. Such a ferrule-like cap has been made from casts of resected normal heads of the radius. By the implantation of these metal replicas it was hoped that, after the joint had been gently cleansed of loose fragments, for the broken or fragmented head could be substituted a nonirritating and nonadhering body of exact shape of the original head which would permit rotation, prevent new bone formation, and in addition maintain complete length of the radius by a normal pressure against the external condyle of the humerus. Thus changes in the distal radioulnar joint subsequent to length loss of the radius and loss of support by impingement against the condyle of the humerus might be avoided. Likewise earlier active use of the elbow after resection

of the head of the radius might be permitted without fear of new bone formation, excessive joint irritation, and subsequent adherences or contractions. These factors taken together might lessen the period of convalescence and insure a higher percentage of functional recovery after lesions supposedly demanding removal of the head of the radius.

Substitute radial head ferrules were first prepared for dogs of medium weight, 15 to 18 pounds, from a cast made of radial heads obtained by operation. The first ferrules were hollow, polished, and were expected to fit quite exactly onto the resected neck of the radius, containing two or more perforations through which small fixation nails or absorbable stitches could maintain attachment to the radius. A second lot had split sides to permit greater ease in molding or bending to fit the variation in size of individual bones at the time of operation, and a third lot were made with an extension center flanged pin for insertion into the medullary canal of the cut-off radius to afford both fixation and correct alinement. A similar evolutionary series of ferrule caps was prepared for use in human elbows.

EXPERIMENTS

A series of experiments on dogs was performed. All dogs were operated upon under nembutal anesthesia, 1 grain to each 5 pounds of weight, by the use of strict asepsis and a constrictor on the foreleg. All dogs' wounds healed *per primam*. They were allowed all freedom of movement, without dressing, immediately after operation.

DOG 1, May 22, 1940, medium sized dog, weight 16 pounds. The head of the right radius was exposed, resected, and a vitallium cap was inserted into the hiatus. This fit fairly well over the upper end of the radius and on rotatory motions of the forepaw was seen to glide satisfactorily against the capitellum of the humerus. The wound was closed in layers with buried catgut and black silk in the skin. The head of the left radius was exposed and resected in a similar manner by the use of a chisel, and the wound was closed without the insertion of any foreign body. Both operations were performed with a constrictor around the upper part of the foreleg. No splints or dressings were used, as I wished the dog to walk on the legs as soon as possible and wished to permit all the irritation this would give.

DOG 2, July 18, 1940, the head of first one radius, then the other, was excised and a vitallium cap implanted in both defects.

DOG 3, September 5, 1940, the head of the left radius was resected and closed in the usual manner. The cap fitted very snugly and, to the best of my ability, in correct axis relationship.

DOG 4, November 12, 1940, the left elbow was opened and the head of the radius resected. The chisel unfortunately perforated the skin of the opposite side. One of the new caps with the projecting pin was applied. The joint was closed and the adventitious opening made by the chisel was likewise sutured. The opposite right elbow was not operated upon.

DOG 5, November 15, 1940, a vitallium cap was applied on the head of one radius; the other head was removed and the joint closed without any further treatment.

Summary. December 11, 1940, all 5 dogs operated upon previous to this date are alive and well. Dog 1 shows no impediment whatsoever in walking. Dog 2 does not use the right forepaw quite normally. He holds it slightly flexed; while he will bear weight on it he will not extend it fully in jumping or playing. The others seem quite normal, especially dog 3, in which there is no evidence of any operative procedure. Dogs 4 and 5 play about without limp or evident distress in the elbow.

On December 11, 1940, the dogs were electrocuted. Examination after the superficial tissues were dissected away from the elbow region showed that all caps were thoroughly encased with fibrous, capsular tissue, and none were projecting out from the elbow joint through the joint covering.

The capsules of the elbow joints over the heads of the radii of dog 1 were split open and reflected so the head of the radius could be viewed clearly. On the capped side the shining, smooth surface of the metal cap remained in perfect condition, with a slight amount of free fluid in the joint and smooth synovial lining. There were no adherences from bands within the joint. There was considerable if not a normal amount of rotatory motion in this capped radius. The second elbow, head of which radius had been resected but no cap inserted, was bonily adherent to the ulna and would permit no rotatory motion (synostosis), although there was practically a normal amount of flexion and extension. There was no great amount of new bone formation around the head of the radius, but there were some intra-articular fibrous adhesive bands.

All elbows were then roentgenographed in an effort to portray the difference between the amount of bone formation on the uncapped and the capped side and any synostosis existing between the ulna and the radius in the uncapped or capped joint.

Résumé of x-ray findings. When the vitallium caps are well placed on the cut-off neck and hold position, the dogs being allowed freedom of exercise immediately after the operation, there is a minimum amount of new bone formation, not tending to overgrow the cap nor to invade the elbow joint. If the ferrule is not accurately applied, it tends to angle after active use of the limb, and bone rapidly develops along the exposed surface of the neck, tending to embrace and help fix the cap in the superior radioulnar space. When the cap is accurately applied and fixed in position with the center pin extension, although the medullary cavity has had to be opened, a minimum amount of new bone develops, and the ferrule fills

in the cavity quite perfectly to maintain full length of the radius without demonstrable injury to the cartilage over the capitellum humeri. Under conditions of accurate apposition of the cap, rotating motion of the radius on the ulna was preserved. And in most instances, even after 7 months' burial in the joint, the articular surface of the ferrule remained free from binding adhesions and in no instance showed intra-articular bands or adhesions to the humerus. The greatest degree of overgrowth of tissue was represented by a thin, pellicle-like, membranous structure, grossly resembling regenerated synovial tissue.

Regardless of accuracy and holding character of fixation, all ferrules became aseptically covered after formalin fixation by a thin, precipitated albumin from the synovial fluid of the joint and tended to become filled with soft, gelatinous granulation tissue, which even in the specimen with cap buried over 7 months (dog 1) showed no tendency to fibrous thickening. When the caps were of the slit type, this tissue within tried to grow out through the slits and unite with the advancing overgrowth of fibrous tissue regenerating from the joint covering.

In contrast, when the head was removed by similar technique and subjected to an equal chance for active use after operation, the control joints of the same dog became the seat of a greater outgrowth of bone which tended to re-form and simulate the removed head in contour. This did not, even in dog 1, 7 months' duration, grow out to full size of the head of the radius, nor did it fully occupy the surface of the joint which formerly held the head of the radius. These control joints showed also a greater amount of fibrous tissue overgrowth, some intra-articular adhesions, and a greater restriction of rotatory motion, in dog 1 amounting to a clinical bony ankylosis between radial neck and sigmoid notch of the ulna.

It was not possible to show in dogs that loss of length developed in the radii which were not supplemented by the ferrule after excision of the head, although the dog actively used the leg over long periods of time. The dog's forearm permits far less rotatory motion at the superior radioulnar joint than does a human elbow, and the two forearm bones are much more closely bound together by the powerful interosseous ligament. Supporting soft tissues including muscle and tendons are tougher and less voluminous, and the leg as a whole has far less proportionate amount of subcutaneous fat than the human forearm.

CASE REPORTS

Case 1. Mrs. Isabelle C., 55 years old, fell May 1, 1940, and injured her right elbow. She was seen first on May 10, 1940, with clinical findings of fracture of the head of the right radius. The roentgenogram showed a comminuted head, angularly displaced at the neck, and a longitudinal split running down the shaft of the bone.

Operation to resect the head and implant the vitallium ferrule was performed on May 10, 1940, a Martin bandage being used on the arm. When the joint was opened, the comminuted head, still attached by a few narrow periosteal shreds, was seen at once to be angulated. The cartilage on the joint surface of the head was completely torn off and lay between the two major bone fragments. The ferrule was fitted over the trimmed neck of the bone as well as could be done, and it was attached by a catgut suture inserted through a drill hole in the bone and tied through the opening in the metal cap. It did not fit very well, as the aperture in the cap was too small. This was one of the first type of ferrules made.

After the wound was closed, no splintage of any kind was employed, but after the forearm was dressed it was held in a sling at right angles to the arm, and active motion was encouraged from the second postoperative day. The wound healed cleanly. The patient left the hospital in 7 days with instructions to continue use short of pain. By June 24, 1940, she could do her regular housework, could extend her forearm to 140 degrees with the arm, and had very slight, if any, pain in elbow. Supination was possible only to a straight line, pronation was three-fourths normal. This condition improved a little, and she kept on using the arm.

On November 7, 1940, flexion of the forearm was normal, extension within 8 degrees of normal. A roentgenogram showed that the ferrule had been displaced away from its seat on the upper end of the radius but still lay in the cavity of the superior radioulnar joint, and that some new bone had formed around the end of the cut-off neck of the radius. There was no pain in the distal radioulnar joint and no evidence of anatomical disturbance of it shown by roentgenological examination, as might follow shortening of the radius.

She re-entered the hospital December 3, 1940, and a second operation was performed the following morning, an entrance being made into the joint via the old scar, which was excised. When the elbow joint was opened a small amount of normal colored synovial fluid was encountered. There was some periarticular fibrosis in the tissues, but the cap was completely enclosed within the joint, and the synovial surface about it was in no place adherent; its surface was smooth and shiny as on the day of implantation 7 months before, and it lifted out with ease. Around the neck of the bone was some newly formed osseous tissue and a contracting, soft, osteoid mass plugging the medullary canal of the bone, which dissected off easily. The neck and newly formed bone were chiseled off quite squarely, and the last made type of ferrule with projecting pin was quite satisfactorily slipped over the bone end after insertion of the point in the slightly reamed out medullary opening. The joint was closed completely and dressed, with no splintage. On December 19, 1940, the wound was completely healed. There was much freer and painless flexion and extension and rotation a little beyond a straight line in supination. This result was much more satisfactory.

The findings in this patient, in whom a misplaced ferrule was removed and replaced by a pin extension ferrule after 7 months, indicate that the human elbow tends to react with less fibrous tissue regeneration than in that of the dog. Her elbow joint showed no intra-articular adhesion, and the ferrule was completely covered and lay within the

joint space, from which it was readily lifted after the scar of original operation had been opened. This was in marked contrast to the findings in dogs, in which the head had to be pried out even though buried only a month.

I have seen in roentgenograms a shadowy outline of apparent regeneration of the head of the radius developing within a year after I have surgically removed the head of the bone. No opportunity has ever been given to study the character of the material causing this shadow, nor to determine whether it resulted from regeneration from the cut-off neck or represented a deposit of calcified material in the wall of that portion of the joint immediately overlying the site of the removed head. Similar regrowths have been reported by Sutrow.

CASE 2. Frank F., 21 years old, shipping clerk, was first seen August 29, 1940, when he fell about 8 feet to a brick pavement with resulting fracture of the left carpal navicular and head of the right radius, along with dislocation of the right ulna at the elbow. The dislocated ulna was reduced. On August 31, 1940, the right elbow joint was opened, a Martin bandage being used on the arm. As the superficial tissues were cut through, local edema was encountered, and when the joint was opened, bloody synovial fluid ran out, and the fractured head of the radius appeared. It was lifted out, the joint searched for any small fragments, and the neck was cut off quite squarely about ¾ inch back from the normal joint ends, the procedure keeping within the elbow joint and avoiding injury of synovial surface and capsule except at the site of entrance incision. Over the end of the radius a vitallium ferrule was quite well fitted and was held in position without suture or additional fixation. The joint was closed, and on account of the recently reduced dislocation of the ulna, the forearm was held at right angles to the arm in full supination in a posterior molded splint, carried in a sling.

A few days later we were able by fluoroscopic examination to make additional diagnosis of a duodenal ulcer and a long retrocecal appendix in this patient following a small bowel hemorrhage. By September 10, 1940, there was good painless rotatory motion in the right forearm. The wound was healed, and the stitches were removed. He was allowed to leave the hospital without splintage on the right arm and was instructed to attempt such active use as caused no pain. On December 17, 1940, he had about 15 degrees of supination beyond the midline and nearly complete flexion. Full extension of the forearm lacked about 12 degrees. There was no great complaint of elbow pain. However, there was a feeling of crepitus when the forearm was rotated, and the thumb pressed over the imbedded cap. Roentgenographic examination showed the cap angled and not on the neck very well. There was a little bone growing up over the ulnar surface of the cap but no excess new bone developing around the head of the radius. There was no disturbance in the distal radioulnar joint.

CASE 3. George H., 31 years old, packer, was first seen on November 1, 1940, and stated that 3 weeks before he had fallen, broken his right elbow and had been treated by the application of a posterior molded plaster-of-Paris splint directly upon the skin, extending down the arm and forearm to the wrist with the forearm in a position of 100 degrees extension with the arm and in slight pronation. This splint was removed with some difficulty, and a roentgenogram showed a fracture of the right olecranon almost at its base with the shaft of the ulna pushed forward and a comminuted fracture of the head of the radius. On account of the condition of the skin about the elbow, operation had to be deferred until November 6, 1940.

After application of a Martin bandage, an incision was made on the outer side of the elbow starting just above the external condyle of the humerus extending down along the shaft of the radius. This was deepened to the elbow joint from which bloody joint fluid escaped. The head of the radius was visualized and was found to be comminuted and severely broken. The fragments were removed, the neck of the bone was smoothed off, and a vitallium cap was inserted with the center pin projecting into the medullary cavity of the bone. A quite snug fit and accurate application were obtained. This incision was closed with catgut in layers and with black waxed silk in the skin. A second incision was made starting near the end of the olecranon process down the shaft of the ulna, which exposed the fracture just below the elbow joint. The fragments of ulna were brought into line, and on the posterior surface was applied a four-screw vitallium plate, which held the main fragments in good alinement but was unable to grasp the intermediate triangular fragment very satisfactorily. This wound was likewise closed in layers, and a plaster-of-Paris dressing was applied from just below the axilla to the base of the fingers with the forearm at right angles to the arm and in full supination.

On December 17, 1940, the plaster was removed; the wounds were cleanly healed. There was little power of pronation or supination. Roentgenogram showed the cap properly in place on the radius. The ulna showed no callus. The arm therefore was replaced in a circular plaster-of-Paris dressing from the base of the fingers to the axilla at right angles to the arm and in supination. He later developed union in the ulna and now has about 50 per cent functional use of the joint.

A question yet to be decided is whether some period of immobilization in a suitable splint is better after application of the metal cap or whether early motion should follow. Will the early motion lessen the amount of joint shrinkage and confining periarticular fibrosis? Apparently the protecting cap does not tend to adhere to the lining of the joint in human beings. It easily and quickly becomes surrounded by a normal appearing synovial surface and of itself causes no pain or distress even when not tightly affixed or adherent to the shaft of the radius. This observation is different from the amount of heavy fibrous enclosure of the ferrule observed in dogs. The ferrule probably does, however, require firm fixation to the end of the radius to display its best effects. It may not require the approximately full size nor the normal anatomical configuration of the head of the radius but may be smaller in circumference than the resected head and easier to insert on that account. It must, however, maintain the anatomical length of the radius.

Apparently the cap should be fitted with a central pin for insertion into the medullary opening of the head of the radius to give both fixation and axial alinement. It should likewise not be

split, certainly not extensively, as this may abet new bone formation or permit outgrowth of new bone from the radial end. A small hole may be left in the skirted end of the cap through which the cap could be fixed to the shaft of the radius by a small indriven screw or nail. Certainly, the human elbow reacts far less violently to the operation for the removal of the head of the radius or the insertion of the cap than does the dog's joint. There is also far less motion and freedom of space in the dog's superior radioulnar joint than in the human elbow. I feel, therefore, that no direct conclusion can be drawn from the greater tendency in these animals for the joint fibrous and cartilaginous tissues to overgrow the buried metal cap in contrast to the experience in the human elbow, where, after more than 7 months of burial, the cap was completely free and lifted out immediately when the joint was opened for the second time.

After these experiences I believe that a device of this character may shorten convalescence and afford a better prognosis for injuries and conditions requiring resection of the head of the radius and attempts to restore the elbow joint to its best function. I believe that shortening of the radius with subsequent changes in the distal radioulnar joint may thus be avoided.

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MALIGNANT THYMOMA

Clinical-pathological Study of Eight Cases

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IN 1916 Ewing stated that "no group of tumors has more successfully resisted attempts at interpretation and classification than those of the thymus." Since then our knowledge of the anatomy of the thymus gland has been advanced, primarily because of the painstaking work of Hammar; erroneous ideas about an internal secretion of the thymus have been corrected by the experiments of Park and McClure; and a number of thymic tumors have been analyzed from the clinical and pathological standpoint. However, there is still so much confusion that Ewing's words might have been written today.

CLASSIFICATION OF THYMOMAS

Pathological classification so necessary to the knowledge of tumors has been particularly difficult for thymic neoplasms. The ambiguous term "thymoma," which includes all malignant thymic tumors, expresses our imperfect knowledge regarding the sources of these tumors. It indicates only that the new-growth originates from the parenchyma of the thymus.

The histogenetic classification of thymic tumors is closely linked with the nature of the thymic cells. It is generally accepted that the reticulum cells of the thymus originate from the entodermal epithelium of the third branchial clefts and that Hassal's corpuscles are degenerative products of the epithelial reticulum. There is no disagreement regarding thymic tumors in which the cells resemble the reticulum cells and tend to form concentric whorls imitating Hassal's bodies. Such tumors are carcinomas.

On the other hand, the nature of the small thymic cells is still being debated. Dantchakoff, Hammar, and Maximow take the view that they are lymphocytes, while Schridde, Bell, and Ewing claim their descent from the epithelium. Ewing questions the existence of a pure lymphocytoma of the thymus and believes that the small round cell tumors of the thymus arise also from the epithelial reticulum. The majority of pathologists, however, follow Hammar and regard the small thymic cells as true lymphocytes. Accepting this view, we classify the small round cell tumors of the thymus as lymphosarcomas.

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The rarity of the thymic tumors has impeded the acquisition of knowledge concerning their structure, clinical course, and response to different forms of treatment. In a series of 10,800 consecutive autopsies performed at the Cook County Hospital, only 4 cases of malignant thymoma were encountered. The largest group of cases recorded by a single observer consisted of 25 thymomas which Symmers found among 17,000 autopsies.

The fact that at St. Francis Hospital 8 cases of thymoma have been observed during the last 6 years suggests that these tumors are not as rare as the scanty reports would indicate.

Regarding the anatomical diagnosis of thymoma, the following facts point to the thymic origin of a mediastinal tumor (Foot): (1) The situation of a large not too lobulated, firm mass at the site of the thymus in the anterior mediastinum; (2) extension downward behind the sternum, without infiltrating the bone; (3) involvement of the pericardium and pleura by direct lymphatic extension; (4) a resemblance to thymic tissue on histological examination. The finding of Hassal's corpuscles is helpful, but not essential.

Many authors have questioned the thymic origin when the diagnosis was based on the location of the tumor, but as Ewing points out, the objections seem to apply chiefly to clinical diagnosis. There is little difficulty in distinguishing thymic tumors at autopsy from tumors of mediastinal lymph nodes, lung, or sternum. They usually surround and compress the trachea, bronchi, heart, and great vessels and cause death by asphyxia and venous obstruction.

LYMPHOSARCOMA

In 1932 Crosby collected from the literature 122 cases of lymphosarcoma of the thymus. As regards sex, there were about double as many cases in males as in females. The eldest patient was 86 years of age, the youngest 4½ months. By far the largest number of tumors occurred before the age of 40 years and many were in children.

Renault, Cathala, and Plichet reported a case of this type which metastasized widely. Lamarque and Bert observed a case of lymphocytoma in which the pathological diagnosis was made from a biopsy of a suprasternal mass which was con-

tinuous with a large mediastinal tumor. Crosby's case of thymic lymphosarcoma occurred in a 33 year old man who died 3 months after the first symptoms. The diagnosis was made at autopsy.

Symmers, Smith, Knutti, Evert, and Harvier regarded their cases as malignant, thymic lymphocytomas, basing their diagnosis on the situation of the tumor and its gross form. In other instances the thymic origin has been further supported by the presence in the tumor of cell groups resembling Hassal's corpuscles (Grandhomme, Helvestine, Coenen, Gerlach).

Very few of the reports on thymic lymphosarcoma contain information as to the reaction to radiation. Singer reported one such tumor which was highly radiosensitive. Janeway's 2 cases of thymic lymphosarcoma regressed under radium treatment but soon recurred. Repeated treatment kept one of his patients alive for 2½ years. In Harvier's case the tumor regressed readily under radiation but recurred so quickly that death resulted in 3 months.

Desjardin's patient was living, with disease still present, after 4 years. Haagensen reported 1 case of malignant lymphocytoma in an Italian boy of 14 years. Treatment with radium emanation was followed by regression of the mediastinal shadow. The fact that death occurred 5 weeks after radiation had been given, however, indicates that this presumed regression must have been very slight. Cutler reported 8 cases of thymic lymphosarcoma in 1935. In only 2 cases did the tumor respond to radiation. One patient was clinically free from disease 7 years after the onset. Another case was in good general condition 2 years after the diagnosis of lymphosarcoma was made.

CASE REPORTS

Case 1. Mrs. M. H., 61 years of age, white, married woman, was admitted to St. Francis Hospital, October 4, 1938. Three weeks before admission, the patient stated she had had pneumonia. Five days ago, she began to have shortness of breath which became progressively worse. She also noticed bloody sputum.

At the time of admission, the patient was cyanotic, and the breathing was rapid and forced. There was no swelling of the lymph nodes of the neck. The expansion of the thorax was limited on the right side and there was dullness to percussion and absence of breath sounds in the lower half of the right chest. The heart was moderately enlarged, the pulse rate was rapid, but regular. There was no edema. Roentgenological examination disclosed a dense cloudiness 3 inches (7.6 cm.) wide on the right border of the sternum, extending from the apex of the right lung to the diaphragm. After aspiration of about 1,000 cubic centimeters of thin, slightly bloody fluid from the right pleural cavity, the x-ray shadow was greatly reduced, and a diagnosis of mediastinal tumor was made. From the presence of lymphocytes and lymphoblasts in the sediment of the pleural fluid a tentative diagnosis of lymphosarcoma was made.

There was a short period of relief after the chest was tapped. Soon however, cyanosis, cough, and dyspnea became increasingly worse, and death occurred November 1, 1938.

Autopsy was performed and when the chest was opened, a large pyramidal mass, lying in the anterior mediastinum, came into view. The growth resembled the thymus in shape. The length was 18 centimeters, the width at the upper end was 6.5 centimeters, at the base 12 centimeters. It was firm in consistency and in color was pinkish-white. The mass was firmly attached to the pericardium, and the anterior surface of the heart was covered with a whitish 15 millimeters thick layer of tumor tissue. The right diaphragm was converted into a nodular hard mass, about 2 centimeters thick. The great blood vessels and bronchi in the upper mediastinum were firmly surrounded with the tumor mass. The right pleural cavity contained about 1,000 cubic centimeters of slightly bloody fluid.

The spleen was not enlarged and there were no tumor nodules noticed in the liver. The retroperitoneal lymph nodes formed a mass about 8 centimeters in diameter. In both kidneys several small nodules were protruding over the surface. They were of whitish color and less than 5 millimeters in diameter.

Microscopic examination of the thymic growth revealed a diffuse proliferation of lymphocytes, which varied in size. The supporting framework was very scanty. No Hassal's corpuscles were found. The metastatic nodules in kidneys and retroperitoneal lymph nodes and the diffuse thickening of the pericardium and pleura consisted of the same uniform overproduction of lymphocytes. The diaphragmatic pleura was covered with a thick layer of tumor cells which had also infiltrated the muscle to a marked degree.

Anatomical diagnosis: Lymphosarcoma of the thymus involving the pericardium, pleura, and diaphragm. Metastases in kidneys and retroperitoneal lymph nodes.

Case 2. C. M., 41 years of age, white, male, was admitted to St. Francis Hospital June 2, 1936. For 7 weeks, he had had attacks of precordial pain without relation to effort. He had been treated for gastric ulcer, but the attacks of pain increased in length and severity. On admission to the hospital a marked swelling of the left side of the neck was noticed. Examination of the chest disclosed dullness and absence of breath sounds over the left lung. The heart sounds were faint, there were no murmurs. The pulse rate was 104 and the blood pressure 120/85. The electrocardiogram showed depression of the ST_1 and ST_2, and an inverted T. These changes were interpreted as suggestive of coronary occlusion. The white blood cell count was 8,300 and the red blood cell count 4,100,000. The hemoglobin (Sahli) was 88 per cent. The Wassermann test was negative. The urine had a specific gravity of 1.022; chemical and microscopic examination were normal.

Roentgenological examination showed a dense cloudiness throughout the left lower half of the chest, suggesting pleural effusion. Fifty cubic centimeters of pleural fluid were obtained. The fluid was slightly bloody, the sediment had 95 per cent lymphocytes. No bacteria were found. Inoculation of the sediment into two guinea pigs did not reveal tuberculosis. Two weeks after admission, the patient became increasingly dyspneic and cyanotic. The left chest was tapped on 6 occasions and, in all, 4,500 cubic centimeters of bloody exudate were withdrawn. There was only temporary relief. From July 2 on the patient was unable to eat and sleep because of dyspnea; he became extremely restless and died July 12, 1936.

At postmortem examination it was found that the supraclavicular lymph nodes on the left side were moderately enlarged. Their cut surface was firm, grayish-white. On removing the sternum, a mass was found corresponding to

the position and form of the thymus. It was triangular in outline with the base downward and measured 3 by 8 by 10 centimeters. It was firmly attached to the anterior surface of the pericardium encasing the heart in a 3 centimeters thick leatherlike layer. Direct extension from the growth covered the parietal pleura at the base of the left lung. The left pleural cavity contained about 400 cubic centimeters of bloody thin fluid. The lung tissue and the bronchi were not invaded. The cut surface of the thymic growth was yellowish-white, without cysts or hemorrhage. There were no secondary deposits in any part of the body. The spleen was of double size, the cut surface was very soft and of grayish-red color.

Microscopic examination of the thymic tumor revealed a cellular growth composed of closely packed lymphocytes. The framework was inconspicuous. In one section several small Hassal's corpuscles were found. In the pericardium and in the pleura covering the left lower lobe of the lung, thick layers of lymphocytes were seen.

Anatomical diagnosis: Lymphosarcoma of the thymus gland, extending to the pericardium and the left pleura.

CASE 3. J. H., 25 years of age, white, male, came to St. Francis Hospital on October 9, 1934. Four days earlier he suffered pain in the cervical region and noticed an enlargement of the neck above the clavicles. He had no difficulty in breathing and had not lost any weight. Physical examination showed a well nourished young man. His left pupil was dilated and did not react to light and accommodation. The tonsils were slightly swollen, the lips were bluish. The veins of the neck were distended. In the supraclavicular region a firm mass was found which did not move with swallowing. The thyroid was not palpable. The patient had a brassy cough. There was dullness from the upper border of the sternum to the fourth intercostal space and extending 6 centimeters lateral from both margins of the sternum. The breath sounds were almost completely absent over this area. The heart beat was outside the midclavicular line. There were no thrills or murmurs. The aortic sounds were distant. The blood pressure was 142/86.

Liver and spleen were not palpable and there were no masses in the abdomen. The axillary and inguinal lymph nodes were not enlarged. The urine was clear, the specific gravity was 1.006, the chemical tests for albumin, sugar, blood, and bile were negative. The red blood cell count was 4,700,000, the white blood cell count 8,100, hemoglobin (Sahli) was 81 per cent. The Wassermann test was negative.

Roentgenological examination disclosed a large dense mass in the upper mediastinum. On October 10, 1934, a small incision was made on the upper border of the sternum. The suprasternal mass was found to extend behind the sternum into the anterior mediastinum. It was firm, not encapsulated, but fairly circumscribed. A triangular piece, measuring 14 by 8 millimeters, was removed for microscopic study.

The tumor was composed of densely packed cells with very little stroma. The cells were of the small lymphocyte type with variation to the large lymphocyte. The nuclei were large and stained dark. Nucleoli were not seen. The cytoplasm was slight, but clearly stained. Few mitoses were found. There were no Hassal's corpuscles or cells suggesting a thymic reticulum present. Few eosinophilic cells were found. The tumor was divided into irregular lobules by vascular septa from which a reticulum ramified between the tumor cells.

Histological diagnosis: Lymphosarcoma.

The patient received intensive treatment with deep x-ray radiation but had only temporary relief. The symptoms of intrathoracic pressure became more and more manifest: cyanosis, dyspnea, edema of the neck and face, cough and pain became progressively worse. The patient's general condition became rapidly worse and he died on April 10, 1935, 6 months after radiation had been begun.

CASE 4. Mrs. T. C., a white married woman, 30 years of age, was admitted to St. Francis Hospital December 28, 1936. Two years previously she had been treated for syphilis. In February, 1935, her tonsils had been removed. Since August, 1936, she has had severe pain in the back radiating down to both arms. Associated with the pain, she had choking sensation, coughing spells, and difficulty in breathing. Swallowing of food became difficult, especially if the food was not chewed well. These complaints were worse at night. At times the patient noticed a large lump appear on the side of the neck.

Physical examination on admission showed a well nourished and well developed white female. There were masses on each side of the neck. The thyroid was not palpable. The thorax was symmetrical; there was an area of dullness, 6 centimeters wide, on each side of the sternum. The breath sounds were diminished. The abdomen was soft and flat. No masses were palpable. The basal metabolic rate was 6 per cent above normal. The red blood cell count was 3,180,000; the white blood cell count 9,150, with 61 per cent segmented leucocytes and 30 per cent lymphocytes. The urine was clear and of straw color. The specific gravity was 1.019; the reaction was acid. The chemical and microscopic findings were normal.

Roentgenological examination showed the heart shadow mostly obscured and there was a wide mediastinal shadow. A barium capsule stopped in the esophagus at the first dorsal vertebra.

A diagnosis of mediastinal tumor was made, but the patient left the hospital refusing x-ray treatment. She returned on March 23, 1937, complaining of abdominal distress. A mass could be palpated in the pelvis and a diagnosis of uterine myoma was made. On March 24, 1937, a laparotomy was performed. Both ovaries were found markedly enlarged, and a third tumor was found attached to the posterior wall of the pelvis. The 3 tumors were removed.

The pathological specimen consisted of 3 solid oval tumors, two with tubes attached. The ovarian masses measured 6.5 by 5 centimeters and 7.5 by 6 centimeters, respectively. The third specimen measured 6 by 3.5 centimeters. The three tumors had an identical, whitish, brain-like cut surface with several cystic areas.

Microscopic examination showed the tumors to be composed of closely packed lymphocytes with some variation in size. The nuclei were hyperchromatic, the nuclear material was evenly distributed, and there were no distinct nucleoli. The stroma consisted of fine strands of connective tissue. The tumor tissue was richly supplied with small capillaries. Several hemorrhagic areas were encountered. In one ovarian tumor a fresh corpus luteum was present.

Histological diagnosis: Lymphosarcoma in both ovaries and in pelvic lymph node.

After recovery from the operation, the patient received intensive courses of deep x-ray radiation of the mediastinal tumor. The symptoms of increased intrathoracic pressure became more and more alarming. A large mass developed in the right side of the chest. Hard tumors appeared in the right axilla and in the right breast. There was marked edema of the upper extremities. In October, 1937, respiration became extremely labored, cyanosis developed, and the patient had to sit up to breathe. She died October 16, 1937, 9 months after onset of her illness.

LEUCOSARCOMATOSIS

In a series of cases a large thymoma with leucemic blood picture has been described (Fabian),

so that leucemia with involvement of the thymus has been recognized as an atypical variety. It was Sternberg who established the term "leucosarcomatosis" and sharply separated it from the ordinary type of leucemia. He believed that it represents a true tumor process. Autopsy in these cases showed, besides generalized swelling of the lymphatic apparatus, a local lymphosarcomatous growth with invasion of surrounding organs. Four of Sternberg's 6 cases of lymphoid leucosarcomatosis had large mediastinal tumors which had the microscopic structure of lymphosarcoma. They involved the pericardium, the great vessels, and lungs. The spleen was often enlarged, and the liver and kidneys showed streaks of infiltration. The primary growth may exist for weeks, months, or years before invasion of blood stream occurs; but when it does involvement is abrupt, and the process advances with astonishing rapidity.

Haagensen's case, in a 59 year old man, embodied the characteristic features of leucosarcomatosis as they have been described by Sternberg. The mediastinal tumor decreased markedly in size under radiation, but the disease was uncontrollable as a whole. Friedlaender and Foot reported a case of malignant small celled thymoma with acute lymphoid leucemia in a 38 year old colored female. Craver and MacComb observed 4 cases of lymphatic leucemia accompanied with marked enlargement of the thymus. In 1 case, light radiation of the thymic tumor caused a drop in the white blood cell count from 58,000 to 1,800. However, the patient, a 6 year old child, died 3 months later. Autopsy revealed a diffuse lymphoma of the thymus with hyperplasia of the tonsils and lymph nodes, and lymphocytic infiltration of the kidneys, spleen, lungs, heart, and liver.

Major's case, a 42 year old female, had a white blood cell count of 41,000 with 65 per cent lymphocytes. At autopsy, a mediastinal tumor, 10 by 7 by 7 centimeters, was found which was composed of lymphocytes and which contained few concentric structures resembling Hassal's corpuscles. Major did not find definite criteria as to whether the thymic tumor or the blood dyscrasia was primary. Margolis, who observed in 28 cases of lymphatic leucemia 4 with thymic tumor, is of the opinion that the tumor represents merely part of the tendency to lymphocytic infiltration of various organs in leucemia. However, Sternberg's separation of leucosarcomatosis from leucemia has been accepted by many pathologists and has served to emphasize that there are different types of lymphocytic proliferation associated with leucemia and that in some cases the process closely approaches a malignant tumor.

CASE 5. Mrs. M. St., a white married woman, 25 years of age, entered St. Francis Hospital on September 30, 1936. About 3 weeks previously she had pain in her stomach region. She got some relief under heat application. There was no loss of appetite and no fever. Shortly afterward, the patient began to cough and had difficulty in breathing. This became progressively worse until she had to sit up in bed. On different occasions, she had bloody sputum. During the last 3 weeks she lost about 10 pounds.

On admission to the hospital the patient appeared well nourished, she had severe pain in the chest. No palpable lymph nodes were found. The thorax was symmetrical. There was an area of dullness over the mediastinum and the left lung. The heart was not enlarged. Pulse rate was 98, the blood pressure was 110/70, and the respiratory rate 20. The spleen and liver were not palpable. The urine had a specific gravity of 1.015, the chemical and microscopic findings were normal. Hemoglobin (Sahli) was 80 per cent, the red blood cell count 3,640,000, the white blood cell count 84,450. The differential count showed 7 per cent segmented leucocytes and 85 per cent lymphocytes with many lymphoblasts. The Wassermann test was negative. Deep x-ray treatment was given over the mediastinum, but the patient failed rapidly, became nauseated, and was unable to eat or sleep. The area of dullness in the chest increased in size, the cyanosis and dyspnea became worse. Finally, intermittent fever developed and the patient expired October 31, 1936, less than 2 months after the onset of the disease.

At postmortem examination the anterior mediastinum was found to be completely occupied by a wedge shaped hard mass which measured 14 by 6 centimeters and extended from the suprasternal notch downward over the surface of the pericardium as far as the diaphragm. It infiltrated the pericardium and the anterior margin of both lungs. The great vessels at the base of the heart were surrounded by the growth, and the large bronchi were completely encased. There were no tumors in the lung tissue nor in the walls of the bronchi. The pleural cavities contained about 500 cubic centimeters of bloody fluid. The spleen was three times normal size, and there was a large anemic infarct on the upper pole. The pulp was soft, homogeneous, grayish-red. The liver was soft, not enlarged and the color of the cut surface was light brown. Lymph node enlargement was encountered only in the mediastinum.

Microscopic examination of the thymic tumor showed the presence of diffuse overgrowth of lymphoid cells. The cells were closely packed and the stroma was scanty. The nucleus of the tumor cells was round, dark stained, and the cytoplasm was nongranular and light stained. No Hassal's corpuscles were seen. In kidney and liver, streaks of lymphocytes were found in the interstitial tissue and the pulp of the spleen had a diffuse hyperplasia of lymphocytes and lymphoblasts. No Malpighian bodies were found.

Anatomical diagnosis: Leucosarcomatosis of the thymus. Invasion of the pericardium and both pleural surfaces. Splenomegaly. Lymphocytic infiltration of liver and kidneys.

HODGKIN'S DISEASE

Hodgkin's disease of the mediastinum is a well identified local form of this disease. At autopsy it is often difficult to state whether the process arises in the lymph nodes or in the thymus since at the time when death occurs, Hassal's corpuscles are, as a rule, no longer found. Ziegler reported 3 cases of this type. The process forms a massive tumor which infiltrates the pleura and the peri-

Fig. 1. Case 1. Thymic lymphosarcoma.

Fig. 2. Case 1. Anterior view of thymic lymphosarcoma involving pericardium.

cardium, and surrounds and compresses the blood vessels, the trachea, and bronchi. There is often involvement of the bronchial and cervical lymph nodes and of the lung tissue. Ewing who, in 1916, reported 3 such cases, regards this type of thymoma as a form of infectious granuloma arising from the epithelial reticulum of the thymus, with many lymphocytes persisting. He found giant cells which were different from those of Hodgkin's disease in other parts of the body. They were very large, the cytoplasm was acidophilic, and the nuclei were hyperchromatic. Ewing separated Hodgkin's disease of the thymus from other forms

Fig. 3. Case 1. Posterior view of thymic lymphosarcoma compressing large vessels and bronchi.

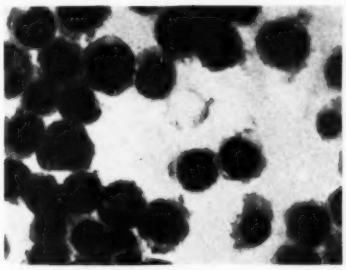


Fig. 4, left. Case 1. Sediment of pleural fluid, showing lymphocytes and lymphoblasts.

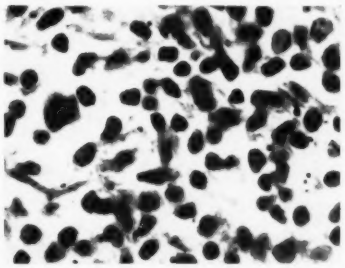


Fig. 5. Case 1. Microscopic section of thymic lymphosarcoma. Marked variation in size and form of cells.

Fig. 6. Case 2. Roentgenogram of thymic lymphosarcoma.

of Hodgkin's disease and attributed its malignancy to its origin from the peculiar reticulum cells of the thymus.

A thymic origin has been most apparent in the observation by Wollstein and McLean in a 4½ months old infant. The thymus was enlarged but free and encapsulated. It showed the typical structure of Hodgkin's disease. The organs immediately surrounding the thymus were not involved, but many abdominal and some thoracic nodes as well as the spleen, liver, and kidneys were infiltrated. Simmons and Benet reported the results of radiation in mediastinal Hodgkin's disease. Although none of their patients was cured, 1 survived for 5 years. Desjardins observed a case with mediastinal Hodgkin's disease in which the tumor had been kept under control 3½ years.

Haagensen's first case of mediastinal Hodgkin's disease, in a 27 year old male, improved markedly under x-ray treatment. He died 4 years after the onset of the illness. At autopsy no trace of the large mediastinal mass was found which roentgenographic studies proved to have existed 3 years previously. In his second case, a 22 year old female, the mediastinal process regressed only partially and very slowly under adequate doses of radiation. The patient died 2 years after the tumor was noticed.

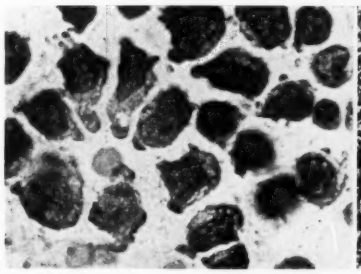
Andrus and Heuer observed a case of thymic Hodgkin's disease in a 15 year old boy. The diagnosis was established by biopsy. Sixteen months after radiation there was no appreciable change in the size of the mediastinal shadow although the density appeared slightly decreased.

In the 5 cases of Hodgkin's disease of the thymus reported by Symmers the patients died from 12 weeks to 3 years after the onset of pressure symptoms. Two of his cases had x-ray treatment without apparent results.

Fig. 7. Case 2. Anterior view of thymic lymphosarcoma, extending to pericardium and left pleura.

CASE 6. H. S., 21 years of age, white, male, was admitted to St. Francis Hospital on July 8, 1938. He had not felt well for the last 9 weeks and had to stay in bed part of the time. He had had chills and fever, had been coughing considerably, and had lost about 30 pounds in weight. On admission to the hospital, his temperature was 104 degrees, his pulse, 132; respiratory rate, 30. His tongue was cherry red with irregular white patches. The glands of the neck were slightly enlarged. The chest expansion was equal, there were coarse râles and increased fremitus over both lungs. The clinical impression was that the patient had an infectious disease. Laboratory tests for malaria, typhoid fever, tuberculosis, and tularemia were negative. The examination of the urine did not show abnormal findings. In the stool were many red blood cells but no parasites were found. The hemoglobin was 8.4 grams; red blood cell count, 2,720,000; white blood cell count, 2,500. There were 2 per cent eosinophilic cells, 3 young forms, 21 band forms, 35 segmented, 37 lymphocytes and 2 monocytes. Kline flocculation test was negative. Roentgenological examination of the chest revealed the pleural angles clear, the heart not enlarged. There was no consolidation of the lungs. The upper mediastinum was wide and dense and the markings of the lung hilus were increased. X-ray study of the colon after barium enema, showed normal filling and normal motility. On July 13, the spleen became palpable 4 centimeters below the costal margin. A clinical diagnosis of Banti's disease was made, and on July 29, laparotomy was performed. The spleen was found to be markedly enlarged. The attempt to remove it was unsuccessful on account of hemorrhage from the friable splenic tissue. The patient expired the following day, 12 weeks after the first symptoms had been noticed.

At postmortem examination it was found that the upper mediastinal region was occupied by a firm whitish tumor which imitated the two lobes of the thymus. The left lobe measured 6 by 3 centimeters and the right 4 by 2 centimeters. The tumor was adherent to the surrounding structures. The peribronchial lymph nodes were enlarged and infiltrated with tumor tissue. No nodules were found in the lungs. The cut surface of the thymic tumor was grayish-



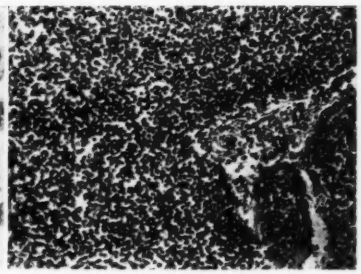


Fig. 8, left. Case 2. Sediment of pleural fluid, consisting of polygonal and round lymphoid cells.

Fig. 9. Case 2. Microscopic section of thymic lympho- sarcoma.

white, there were irregular brown and hemorrhagic areas. The heart was small and not involved in the tumor process. The cervical lymph nodes were moderately enlarged and of firm consistency. The spleen weighed more than 500 grams and the capsule was ruptured at the lateral margin. There was a large hematoma surrounding the spleen. The cut surface of the spleen was purplish-red, and there were many whitish nodules, from 1 to 3 centimeters in diameter, protruding over the cut surface. The mesenteric glands were of normal size, but the retroperitoneal lymph nodes were markedly enlarged and had a firm grayish-white cut surface.

Microscopic examination showed the thymic tumor to be composed of a diffuse proliferation of reticulum cells, lymphocytes, and giant cells of the Sternberg-Reed type. Necrosis and fibrosis were present in many sections. Eosinophilic cells were scanty in the mediastinal growth, but abundant in the bone marrow of ribs and vertebrae which were infiltrated with typical Hodgkin's tissue. The nodules in the spleen and in the retroperitoneal lymph nodes also had the histological structure of Hodgkin's disease. In the periportal tissue of the liver few areas of cellular proliferation were found. The most important cell types in all these lesions were large rounded cells with clear protoplasm and single or multilobed hyperchromatic nuclei.

Fig. 10. Case 3. Roentgenogram of thymic lymphosarcoma.

Case 7. Mrs. J. H. R., a middle aged white woman, complained on August 10, 1937, of an itching eczema below the right nipple. It formed a scale and when peeled off, left a raw, pink colored area, about 1 centimeter in diameter. This lesion recurred time and time again and resulted in discoloration and thickening of the skin. Three physicians saw this patient and made a tentative diagnosis of Paget's disease. Dr. E. E. Talley, on December 10, 1938, removed a piece of skin for examination. Microscopic examination showed proliferation of the epidermis with elongation of rete pegs. The cells were well differentiated and did not show the characteristics of Paget's disease. The corium was densely infiltrated with round cells which had the appearance of lymphocytes and plasma cells. No eosinophilic cells or Sternberg-Reed cells were found. The microscopic diagnosis was: chronic dermatitis. After this biopsy, the patient felt very well. She gained in weight up to 211 pounds by December, 1939. When her physician saw her again in September, 1940, her weight had decreased to 175 pounds, and she was very weak, tired easily, and her skin was pale. Hemoglobin was 65 per cent, the red blood cell count 3,450,000. Roentgenological examination of the chest revealed a large mass in the upper mediastinum extending 7 to 8 centimeters to both sides from the sternum. The mass was not pulsating. The heart was slightly enlarged. The Wassermann test was negative. The only symptoms of increased intrathoracic pressure were cough and some pain in the left shoulder. On the patient's hands and arms, and on the back of her neck, indurated, raised, pink areas appeared

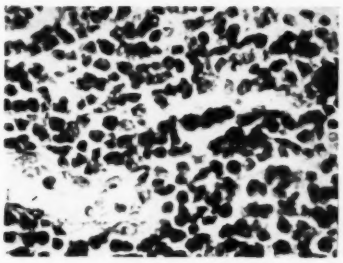


Fig. 11. Case 3. Microscopic section of biopsy specimen.

Fig. 12. Case 4. Metastases of thymic lymphosarcoma in both ovaries and in pelvic lymph node.

about 0.5 to 1 centimeter in diameter. There was no itching. These areas were similar in appearance to the skin lesion near the nipple removed in 1938. On December 11, 1940, her physician removed a hard lymph node from the neck. It measured 2 by 1.2 centimeters and had on cross section a homogeneous whitish appearance. Microscopic examination showed complete obliteration of the normal structure of the lymph node. There was a diffuse growth of lymphocytes and polygonal, pale reticulum cells. These large cells had a vesicular nucleus and a tendency to form a syncytium. Several giant cells with one or several dark stained nuclei were present and few eosinophilic cells were encountered. There was no evidence of necrosis or fibrosis in the lymph node.

Histological diagnosis: Hodgkin's disease.

From the clinical, roentgenological and histological findings the case was interpreted as thymic Hodgkin's disease with manifestations of the disease in skin and cervical lymph nodes.

CARCINOMA

Carcinoma is the rarest form of malignant thymoma. It originates from the epithelial reticulum of the thymus and consists of sheets and strands of epithelial cells lying in a dense connective tissue stroma. The tumor cells tend to be flat, vary in size and shape, and may form concentric whorls resembling Hassal's corpuscles, not only in the primary growth, but also in metastases.

The best examples of this type have been reported by Symmers and Vance, Jacobson, Foot, Margolis, Obiditsch, and Brannan. More common are the forms of thymic carcinoma which are made up of two types of cells; flat epithelial cells

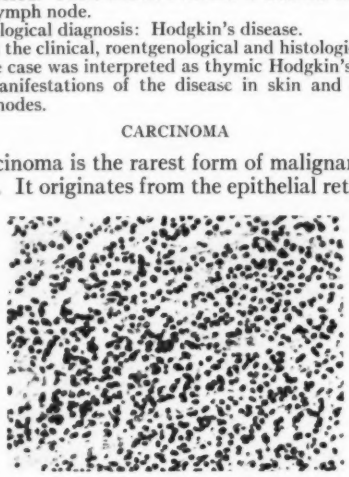


Fig. 13. Case 4. Microscopic section of ovarian tumor.

Fig. 14. Case 4. Roentgenogram of primary lymphosarcoma in thymus.

Fig. 15. Case 5. Leucosarcomatosis of thymus, involving pericardium and both pleural surfaces.

originating from the thymic reticulum, and lymphoid cells which are derived from the small thymic cells. The structure of these tumors is identical with that of the lympho-epitheliomas which occur in or around the pharynx. Matras and Priesel discussed this form of malignant thymoma and reported 7 cases of their own. The same type was described by Rubaschow, Largiadér, and Schmidtmann.

In 1932, Crosby collected from the literature

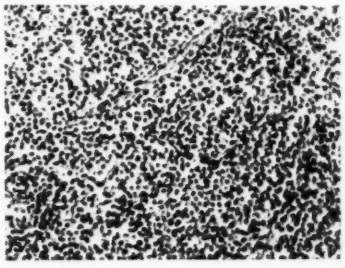


Fig. 16. Case 5. Microscopic section of thymic leucosarcomatosis.

Fig. 17. Case 6. Anterior view of Hodgkin's disease of the thymus.

36 cases of thymic carcinoma with autopsy reports. As regards sex, 25 occurred in males and 10 in females. In one case report the sex was not stated. The majority of cases occurred after the age of forty. The oldest patient was 72 years old, while in 1 case the tumor was found at birth. The tissues in close proximity to the thymus were almost always invaded. In 3 of the cases of thymic carcinoma no metastases were found. While uncommon below the diaphragm, meta-

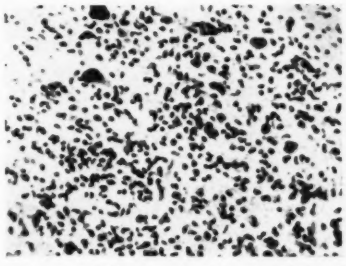


Fig. 18. Case 6. Microscopic structure of thymic Hodgkin's disease. Sternberg-Reed cells are numerous.

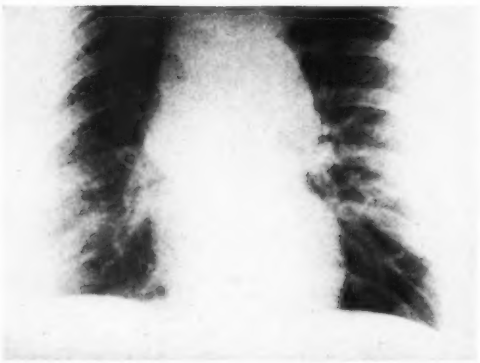


Fig. 19. Case 7. Roentgenogram of Hodgkin's disease of the thymus.

stases may take place to almost any organ of the body.

The information concerning the reaction of thymic carcinoma to radiation is meager. In the case reported by Foot, weekly irradiation with deep x-ray had no apparent effect on the tumor. Lenk described an epithelioma of the thymus, proved by autopsy, which showed no change following intensive radiation. Haagensen's 2 cases of anaplastic carcinoma of the thymus were definitely radioresistant. Although heavily irradiated they decreased but slightly in size, and death occurred in short time. Cutler reported a case of thymic carcinoma in a 56 year old man who in spite of two courses of high voltage roentgen therapy did not show any improvement.

In a number of cases, operative removal of thymic carcinoma has been attempted (Margolis), without success.

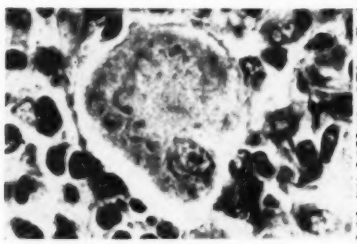
CASE 8. Mrs. P. S., a white married woman, 23 years of age, entered St. Francis Hospital on September 26, 1939. Three weeks previously the patient had cough, dyspnea, and pain in the chest radiating to the left axilla and left side of the neck. She had some fever and became anemic. There was enlargement of lymph nodes in the left cervical region and in the left axilla. Her white blood cell count was 10,000, without changes in the differential count. The pulse was 120, the temperature 97 degrees, and the pulse rate 26. A lymph node was removed for examination from the left side of the neck. It measured 2 by 1.6 centimeters, was hard, and had a grayish cut surface. Microscopic examination revealed a peculiar structure, difficult to interpret. While some areas resembled Hodgkin's disease, others were more in favor of a diagnosis of carcinoma. There were sheets and cords of large flat or polyhedral cells lying in dense connective tissue. Several concentric layers of cells were found which formed whorl-like structures resembling Hassal's corpuscles. Lymphocytes, plasma cells, and eosinophilic cells were irregularly distributed. Many giant cells were found with opaque acidophilic cytoplasm and dark, vesicular nucleus.

Roentgenological examination of the chest revealed a large area of increased density in the mediastinal region extending to the left. Its central portion was very dense, at the left there were mottled areas of lesser density. The shadow was broadest at the level of the left fourth interspace. Its edges were irregular.

Deep x-ray treatment was given to the mediastinal tumor, and there was evidence of improvement. The patient returned home and soon marked exacerbation of symptoms occurred. There was increased dyspnea, cough and pain. The superficial veins of the chest became engorged, edema of the face and of the left arm developed. The area of mediastinal dullness widened; signs of fluid showed in both pleural cavities. Her general condition grew rapidly worse; she died April 23, 1940, 8 months after first symptoms.

At postmortem examination it was disclosed that the right diaphragm was in the level of the sixth, and the left in the seventh intercostal space. Both pleural cavities contained about 2,000 cubic centimeters of clear amber fluid. There were 150 cubic centimeters of light brown fluid in the pericardial sac. When the sternum was removed, a large hard mass was found to extend from the suprasternal notch to the upper half of the pericardium. The tumor had the form of the thymus gland, was 12 centimeters wide and weighed 850 grams. Trachea, esophagus, and the right and left bronchus were firmly surrounded by the tumor. The great blood vessels at the base of the heart and the auricles were compressed by the extension of the growth into the pericardium. Several small hard nodules, 1 to 2 centimeters in diameter, were found at the surface of the right and left upper lobe of the lungs. The lung tissue itself was not invaded. Cross section of the thymic tumor revealed a hard, whitish tissue with small yellowish areas.

In the peritoneal cavity 1,500 cubic centimeters of amber fluid was found. The peritoneum was glistening and without tumor nodules. Liver, kidneys, adrenals, and pelvic organs were free from tumor. The spleen weighed 170



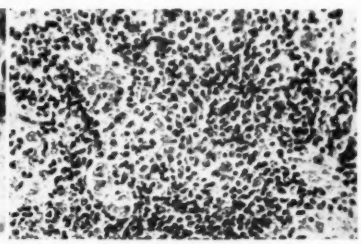


Fig. 20, left. Case 7. Giant cell.
Fig. 21. Characteristic structure of lymph node in case of thymic Hodgkin's disease.

Fig. 22. Case 8. Roentgenogram of carcinoma of the thymus.

Fig. 23. Case 8. Anterior view of thymic carcinoma.

grams and the consistency was firm, the color of the cut surface was purplish. There was no enlargement of the retroperitoneal lymph nodes. The cervical and axillary lymph nodes were hard, small, and whitish on cross section.

Microscopic examination revealed large areas of fibrosis prevailing in the center of the mediastinal tumor. The histological character of the growth became apparent only after examining the peripheral areas and the metastatic nodules in the pleura. The predominating cells were flat, irregular in shape, and characterized by pale staining protoplasm, and a large vesicular nucleus. In places these epithelial reticulum cells occurred singly in a dense fibrous stroma; in others they were arranged in sheets, cords and large islands. A striking feature was a tendency of these large epithelial cells to concentric arrangement and whorl formation, imitating the structure of Hassal's corpuscles. There was admixture of lymphocytes, plasma cells and a few eosinophilic leucocytes. The structure of the tumor corresponded to the description of thymic carcinoma as observed by Foot, Symmers, Margolis.

Histological diagnosis: carcinoma of the thymus, invading the pericardium. Metastases in both pleural cavities.

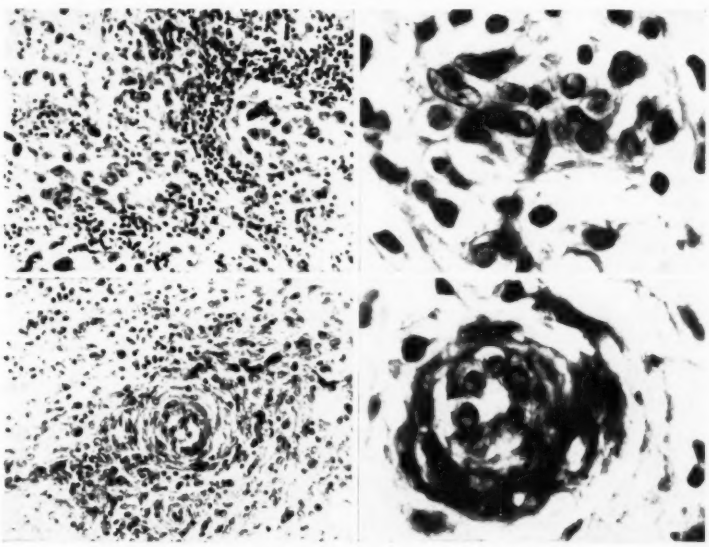


Fig. 24, left. Case 8. Microscopic section of carcinoma of the thymus, composed of epithelial reticulum cells. Tendency to form structures resembling Hassal's corpuscles.

Fig. 25. Case 8. High magnification of thymic carcinoma. Hassal's corpuscle in lower part.

FACTS FROM OUR CASES

After the developmental anatomy of the thymus has been established (Hammar), it is feasible to classify the thymomas on a histogenetic basis. In my series, 4 different types of malignant thymoma were represented, namely: 4 lymphosarcomas, 1 lymphoid leucosarcomatosis, 2 cases of Hodgkin's disease, and 1 case of carcinoma of the thymus.

Of the 5 cases in which complete autopsy was performed all showed invasion of the pericardium, 3 also of the heart muscle. The pleura was invaded by 2 lymphosarcomas and by the thymic carcinoma. This invasion was either diffuse, or there were circumscribed round nodules. In the first case, the diaphragm was converted into a board-like structure, 1 centimeter thick. In all 5 cases the large bronchi were buried in tumor tissue, but in no case was the mucosa of the bronchi invaded.

Four of the patients died within 5 to 13 weeks after the first pressure symptoms had been noticed; the anatomical findings in these cases indicated that the growth must have existed for a much longer time. The absence of early symptoms is characteristic of thymic tumors. They may expand locally and infiltrate the surrounding tissues with such extension that one is amazed at how the body could withstand the mediastinal growth so long without obvious symptoms. Only after anatomical compensation has been exhausted, pressure signs become apparent and then advance rapidly, causing death within a few weeks.

Early diagnosis of the type of thymic tumor is as difficult as it is imperative from the standpoint of prognosis and treatment. If it be shown that the lesion is a lymphosarcoma or Hodgkin's disease, radiation may give at least temporary relief. Carcinoma of the thymus, on the other hand, is at present hopeless from the onset.

Intermittent dyspnea, hoarseness, or cough in association with dullness on either side of the sternum demand exhaustive roentgenological examination of the chest. The roentgenogram is perhaps the most important single aid in deciding whether a mediastinal tumor is benign or malignant. According to Lenk, the x-ray shadow in lymphosarcoma has an irregular and hazy contour. The organs of the mediastinum are usually not displaced. In Hodgkin's disease the contour is more often clear cut and the evidence of infiltrative growth is less marked. Lenk has been impressed by the fact that in thymic carcinoma the tumor shadow has been broader than long, and that the displacement of the trachea is more frequent than in other malignant mediastinal tumors.

The accurate diagnosis of the various types of thymoma depends on microscopic investigation of tumor tissue which may be accessible to removal. A histological diagnosis during life was made in 6 of our 8 cases. In 3 patients enlarged supraclavicular lymph nodes were removed for biopsy, in 2 lymphosarcomas the cytological study of pleural fluid led to the correct diagnosis and in 1 case the removal of ovarian tumors which were thought to be independent from the mediastinal tumor, proved to be metastases of lymphosarcoma.

Although few radiated cases in which the histological type of thymoma was established have been reported, it seems probable that the reaction of mediastinal tumors to a test dose of radiation may be of value in their differential diagnosis. Lenk and Haagensen presented complete data regarding radiosensitivity of mediastinal tumors in which the pathological nature of the tumor was determined by microscopic examination. From their experience it may be said that lymphosarcoma and leucemic lymphoma are often strikingly radiosensitive although occasionally radioresistant cases are found. Thymic carcinoma and the various benign neoplasms of the mediastinum are radioresistant. More case reports in which the diagnosis has been proved histologically are needed.

Of our 8 cases, 5 patients received adequate radiation. One patient with Hodgkin's disease is alive 2 years after onset of the disease; the patient with thymic carcinoma received temporary relief after heavy deep x-ray therapy, but died 9 months after the first symptoms appeared. The 3 patients with lymphosarcoma did not respond as well to radiation as was expected from the literature. After a short period of relief, the pressure symptoms increased rapidly, and the patients died 5 weeks, 6 months and 9 months, respectively, after onset of the disease.

SUMMARY

1. A comparative clinical-pathological study of 8 cases of thymoma is reported.

2. As the histogenesis of the thymus gland has been established by the work of Hammar, thymomas can be divided into two groups, namely, those originating from lymphoid tissue and those derived from the epithelial reticulum of the thymus.

3. In the present series there were 5 lymphosarcomas, 1 lymphoid leucosarcomatosis, 2 cases of Hodgkin's disease, and 1 thymic carcinoma.

4. Differential diagnosis between malignant thymoma and benign mediastinal tumors is imperative, since successful removal of the latter has been recorded. The differential diagnosis of the various pathological types of thymic tumor is of practical value because some can be temporarily controlled by radiation.

5. There is no clinical or roentgenological sign to differentiate accurately between the different types of malignant thymoma. Exact diagnosis depends on microscopic study of tumor tissue which may be accessible to biopsy.

6. While thymomas originating from lymphoid tissue are more radiosensitive than thymic carcinoma, at the present no cure has been obtained in either group.

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COMMON BILE DUCT PERISTALSIS

Preliminary Report

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A SEARCH of the literature reveals that there is no record of common duct peristalsis having been observed in man. The present report has to do with such an observation. This was clearly visualized under the fluoroscope as an accidental finding, while a study was being made of a pathological common duct, and it was immediately recorded by pictures. This finding is of more than academic interest. Explanations and descriptions accompany the figures.

This study will be continued as soon as conditions permit. The present case is reported because war conditions are such that thorough and complete investigation cannot now be carried out.

The accompanying pictures show clearly and conclusively that there are changes in the internal diameter of the common bile duct. What are the possible causes? They are (1) changes in intra-abdominal pressure; (2) changes in pressure or position of organs lying alongside; (3) changes in pressure from without (through tube); (4) drugs (amyl nitrite); (5) irritation by the T tube; (6) sphincter of Oddi tissue extending into the duct; and (7) actual peristalsis. Because the location of the changes is in the distal end of the duct, which is retroperitoneal, the first two are not likely. The tube was clamped, and drugs were not used. Hence

Fig. 1

Fig. 2

Fig. 1. Cholangiogram made 10 minutes after ¼ grain of morphine had been given, and approximately 3 minutes after the injection of 15 cubic centimeters of lipidol. In this figure the dye is observed just beginning to enter the duodenum. The interpretation of this picture by itself would indicate either a ductal or pancreatic pathological condition. This entire narrow channel is not a single constriction. It is longer than the areas seen by fluoroscope. If it is all constriction it is not the same as intestinal peristalsis, but, judging from the subsequent pictures, only the upper part is involved.

Fig. 2. Cholangiogram made 2 minutes after Figure 1, and 5 minutes after the injection of the dye. More dye has entered the duodenum. The outline indicates that the distal end of the duct has completely closed. The hepatic ducts are well filled.

Fig. 3

Fig. 4

Fig. 3. Approximately 5 minutes later. The distal end of the duct is open and the contrast medium is flowing freely into the duodenum. The hepatic ducts are almost empty compared with Figure 2, because this area is the source of the enlarged duodenal content.

Fig. 4. The duct is now closing. The T-tube is almost empty. All pictures show a point of leakage at the entrance of the tube into the duct. This had disappeared the next day; it probably drained through the sinus. Notice that the dye is flowing cephalad. This is a good example of reverse duodenal peristalsis which Ivy believes is a cause of biliary stasis. It is not uncommon to see the dye, during serial cholangiograms or by fluoroscope, first traveling in an antiperistaltic direction, then changing to normal. On one occasion the dye did actually enter the pyloric antrum.

the only three possibilities are irritation by the tube (foreign body); contraction of sphincter muscle, and active peristalsis. Irritation could not produce such changes unless the inherent ability to contract and relax was present; the sphincter muscle is affected by morphine and this must therefore be considered, but it is unusual for sphincter tissue to extend so far up the duct—unless the duct passes through the duodenal wall for an abnormally long distance. It is therefore concluded that in this particular patient the common bile duct has the ability to move its contents onward by active effort. The writer has no doubt about this, because the fluoroscopic study showed distinctly and clearly that the shadow of the dye was changed in shape by a temporary constriction, and that a segment of lipidol distal to the constriction was rushed forward into the duodenum. It was because of this that serial pictures were taken. The areas of constriction, as seen under the fluoroscope, were not "caught" in the pictures. This was not due to "milking" by the duodenum, because the constriction was one inch away from the end of the duct as determined by the shadow in the picture.

Peristalsis is activated and excessive proximal to any obstruction in a hollow tube. In this instance a partial obstruction is artificially produced by morphine. *But*, peristalsis cannot be activated unless it is present in either an active or a latent form.

Should we expect to find peristalsis in the common duct? I think so. Why? Because this duct is an integral part of one of the most important

physiological functions of the body and an uninterrupted onward flow of bile is essential to good health. There must be some mechanism, other than just back pressure, to overcome transient states of obstruction. I do not believe that the common bile duct is an inactive, inert, impassive, and immobile hollow tube. This case report indicates that such is not the case.

One of many clinical applications of this finding is that serial cholangiographs should be taken, because the interpretations of single and serial plates will differ. The latter will, of course, be more correct; the single plate may be misleading. (See Figs. 1 to 4).

SUMMARY

A singular observation, never before observed, is recorded because it *indicates* that the common duct of man has the inherent ability to propel its contents forward. The mechanism of this peristalsis is not discussed. A more extensive report will follow.

ACROMIOCLAVICULAR SEPARATION

New Method of Repair

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ACROMIOCLAVICULAR separation may be a seriously disabling injury, due to coincidental tearing of the coracoclavicular ligament. This ligament may be likened to a stout cord by which the scapula, and with it the whole upper extremity, is suspended from the outer end of the clavicle. If this cord be ruptured, the arm drops helplessly to the side and the tip of the clavicle projects upward, tenting the skin over it.

Anatomically, the acromioclavicular articulation is a weak spot at a point of great stress (Fig. 1). Upon it are focused the antagonistic actions of powerful muscle groups, plus the weight of the upper extremity and the added strain of lifting and pulling. The joint surfaces are small, flattened, and obliquely placed, that of the clavicle facing downward and backward. A joint cartilage may or may not be present. The capsular ligaments are not strong and the joint would be dislocated far more frequently were it not for the coracoclavicular ligament. This structure has two groups of short tough fibers, the conoid and trapezoid ligaments, so placed as to reinforce the joint no matter in what direction it moves.

Motion in this joint may be of almost any type but is always very slight, being checked by the coracoclavicular ligament. As Codman has pointed out, "Nature made it slightly movable in order that it might: (1) swing a little . . . (2) rock a little . . . (3) twist a little . . . (4) slide a little inward . . . (5) act like a hinge." Although perfect shoulder motion requires a movable acromioclavicular articulation, fusion of the joint will not embarrass ordinary shoulder function. As a matter of fact, during unrestricted motion of the upper extremity in all directions the acromion moves to such a slight extent upon the clavicle that, in a recent fluoroscopic study of several thousand shoulders, I was never able to detect the exact extent of acromioclavicular motion (1).

Injury usually results from a direct blow upon the acromion, as from a fall. Treatment aims at re-establishment of the integrity of the coracoclavicular ligament or substituting therefor some other means of support between scapula and clavicle. Various slings, harnesses, and dressings have been devised to support the arm and depress the outer end of the clavicle. They all necessitate severe restriction of shoulder joint motion for a considerable period of time and, in cases of complete disruption, fail to re-establish adequate support (Fig. 7a).

Numerous operative procedures have been recommended. Perhaps the one most commonly employed has been that of looping a strip of autogenous fascia under the coracoid process and over or through the clavicle. This is a major operative procedure which requires a general anesthesia, two separate good sized incisions, and a prolonged hospitalization. Even in experienced hands it is a technically difficult operation, involving considerable trauma and attended by definite risks. In optimal cases, recovery is slow and rehabilitation prolonged. Other materials, such as silk and wire, have been used instead of fascia but have

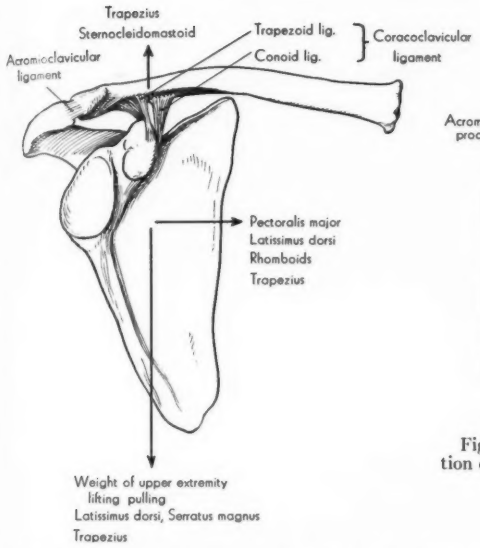


Fig. 1. Forces acting upon the acromioclavicular joint.

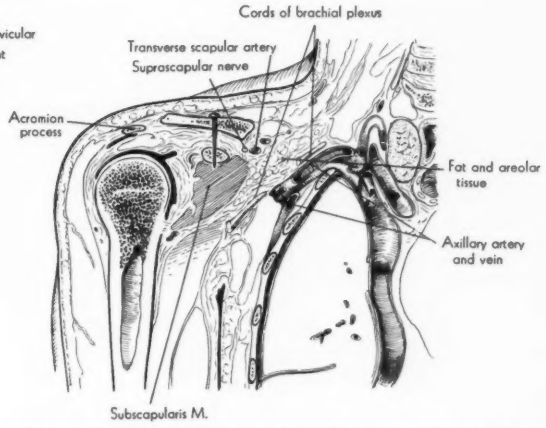


Fig. 3. Coronal section through head of humerus to show relation of screw to important structures.

been unsatisfactory as they tend to cut through the bone. Frozen shoulder is not an uncommon complication.

Recently there has been reported (3) successful fixation of scapula to clavicle by passing Kirschner wires horizontally through the acromion into the clavicle. These are allowed to protrude through the skin and are removed when healing of the ligaments is thought to have taken place. Certain objections may be raised to this procedure. It is not a simple matter to insert flexible wires accurately through the acromion and clavicle in the plane of their thinnest dimensions. To give adequate support, more than one wire must be inserted. The wires may work loose due to bone absorption and active motion. Protrusion of the wires through the skin for several weeks entails a certain risk of infection. Theoretically at least, passage of even small gauge wires through the acromioclavicular joint would predispose to a localized arthritis of this joint. Finally, the wires must subsequently be withdrawn and full reliance for support be placed upon scar formation between the torn ends of the ruptured ligaments.

So far as is known, the method about to be described has never before been used. It consists

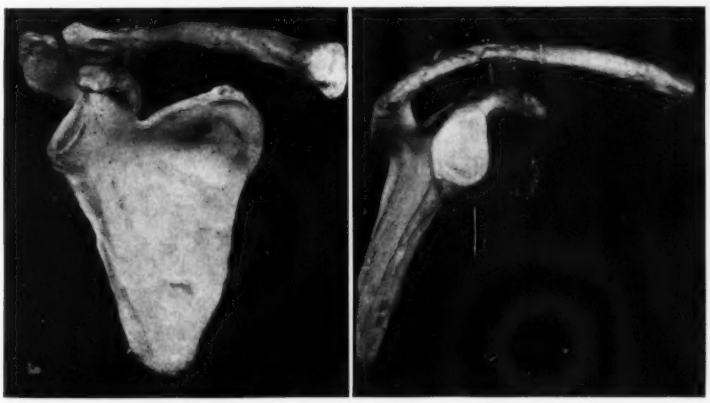
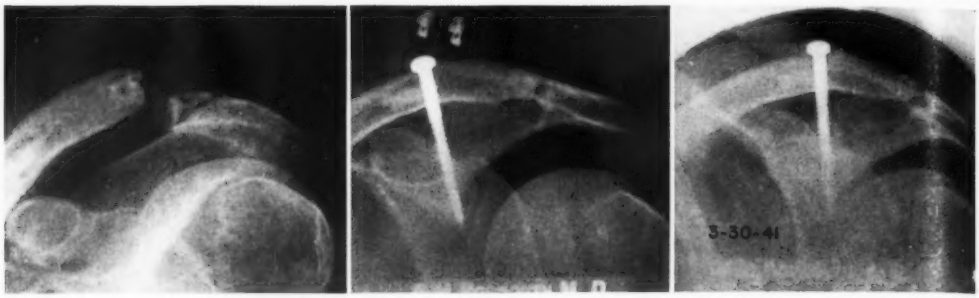


Fig. 2. Author's method of suspending scapula from clavicle by single vitallium screw.



a b c

Fig. 4. P. B., aged 74 years, housewife. a, Roentgenogram taken before operation. b, After reduction with screw. c, 4 months after operation. Note new bone forming about screw.

of suspending the scapula from the clavicle by a single vitallium screw, passed through the clavicle into the coracoid, through a small incision under local anesthesia (Fig. 2).

With the patient seated upright in a chair, the acromioclavicular articulation is infiltrated with 1 per cent novocain. Infiltration is continued, to include the tissues overlying the outer 2 or 3 inches of the clavicle. A ¾ inch incision is then made through the skin, subcutaneous tissues, and periosteum, parallel to and over the outer portion of the clavicle, about 1½ inches proximal to its outer end. This point is marked, upon fluoroscopic examination prior to operation, as the site at which the clavicle directly overlies the coracoid process.

A 3/16 inch hole is then drilled downward through the upper cortex of the clavicle and, after the injection of novocain, through the lower cortex. More novocain is infiltrated through this hole into the underlying torn fibers of the coracoclavicular ligament and also into the periosteum at the base of the coracoid process of the scapula. At this stage of the procedure reduction of the dislocation should be secured and maintained by an assistant who supports the arm and depresses the tip of the clavicle. The upper cortex of the coracoid process can now be outlined rather well with the point of the infiltrating needle, and its position can be checked with a portable fluoroscope previously set up. A hole is then started with a sharp-pointed awl in the upper cortex of the coracoid process, after which a vitallium screw of proper length is inserted through the clavicle into the coracoid process. As the coracoid is relatively soft bone with a thin cortex, the screw easily cuts its own way through the bone without the necessity of previous drilling.

Fig. 5. M. B., aged 73 years, housewife. a, left, Before operation. b, After reduction with screw.

Fig. 6a

Fig. 6b

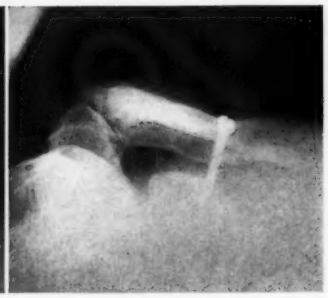


Fig. 6c

Fig. 6. J. M., aged 65 years, laborer. a, Right shoulder before operation. b, Normal left shoulder. c, Reduction apparently complete. d, Roentgenogram from a different angle shows reduction is actually partial, although clinically satisfactory.

Fig. 6d

The hole in the clavicle is purposely made a bit larger than the screw so as to allow free play of the screw within the clavicle. In this way the scapula can be suspended without fixing it rigidly to the clavicle, and a certain degree of motion in all directions can be preserved in the acromioclavicular joint. It is important that reduction of the acromioclavicular separation be maintained until the screw is actually in position. Failure to observe this precaution may result in a misplaced screw or pulling of the screw. Care must also be taken to have the screw penetrate both cortices of the coracoid process, to provide a strong grip on that bone.

Fortunately, no important structures are endangered by this operation (Fig. 3). The axillary vessels and the cords of the brachial plexus lie in an anterior plane deeply medial to the base of the coracoid process when the arm is at the side and are separated from the anterior surface of the subscapularis muscle by a considerable amount of fatty and areolar tissue. As the arm is elevated in the coronal plane, the vessels and nerves tend to approach the tip of the coracoid but are held forward from its base by the intervening subscapularis muscle and tendon. The transverse scapular vessels and the suprascapular nerve pass medial to the base of the coracoid process and so are well out of harm's way. The cephalic vein and deltoid artery lie in an anterior and superficial plane. If the screw, when properly placed, should project through the undersurface of the coracoid process near its base, it will merely bury itself in the fibers of the subscapularis. This has been proved by repeated experiments on the cadaver, in which the screw has been introduced blindly and its position checked by subsequent dissection.

No hemostasis is required and the wound is simply closed with 2 or 3 skin clips or sutures. The operation should be performed in a hospital where adequate facilities and assistance are available, but the patient need not be admitted to the hospital and may be allowed to go home soon after the operation is completed. No sling or other support is necessary; in my opinion, it is contraindicated. Active use of the hand and arm is desired and should be encouraged from the start, but the patient must be warned against lifting or pulling

Fig. 7. A. M., aged 34 years, masseuse. a, left, Preoperative roentgenogram shows failure of pressure dressing to maintain reduction. b, Screw reduction successful.

for at least 8 weeks. If the shoulder should ache or the arm become tired, prompt relief may be secured by resting the elbow on a pillow for a few moments. Frequent gentle exercises are prescribed, to be performed within pain limits. The most useful of these are the arm-swinging exercise of Codman and "crawling up the wall." No passive exercises or manipulation should be done. Physiotherapy, consisting of baking or diathermy, may be employed if desired but it is not essential.

The screw is left in place indefinitely unless some indication arises for its removal. A brief report of 4 cases in which this method has been employed follows.

CASE REPORTS

CASE 1. P. B., aged 74 years, slipped on the stairs, grasped the rail with her left hand to save herself and fell to the floor, striking on the point of her right shoulder. She experienced immediate severe pain in the right shoulder and total loss of use of the right upper extremity. Pain in the shoulder and inability to get in a comfortable position in bed precluded sleep that night. When first seen on the following day, the patient carried the right arm close to her side, with the flexed forearm supported by her left hand. She was in obvious pain and this was greatly aggravated by the slightest motion of the right shoulder. The outer end of the right clavicle projected well above the level of the acromion process of the scapula and there were acute tenderness and preternatural mobility of the acromioclavicular articulation. Diagnosis of acromioclavicular separation was confirmed by fluoroscopic and roentgen examination (Fig. 4). A sling was fitted and mild analgesics prescribed.

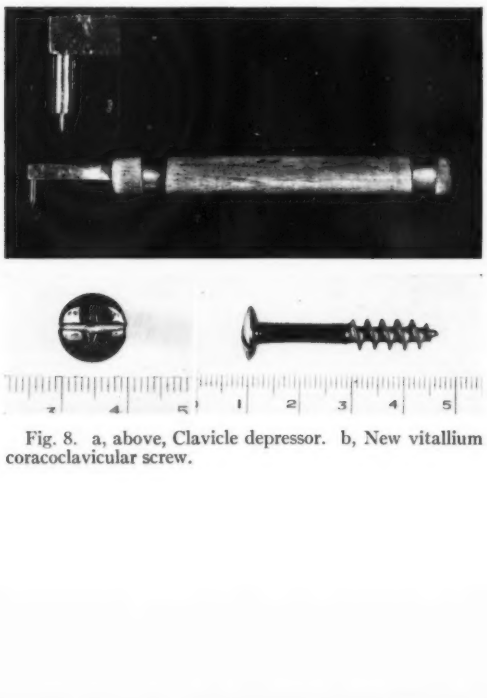


Fig. 8. a, above, Clavicle depressor. b, New vitallium coracoclavicular screw.

This case was complicated by the presence of advanced hypertrophic osteoarthritis, most marked in the joints of the right hand and wrist, and by the fact that the patient was still convalescing from the effects of a right Colles fracture sustained only 2½ months prior to the present injury. Since the severe shoulder pain persisted in spite of the sling and the arthritis rapidly became worse because of it, it was felt that some form of internal support which would at once relieve the pain and free the upper extremity for motion within a reasonable range was demanded. Accordingly, 4 days after injury repair was effected in the manner described. Within 2 weeks of operation the patient was able to feed and dress herself entirely without assistance. From the time of operation there was complete relief from acute pain; the only complaints were of a heaviness in the shoulder and a slight ache when the arm became overtired from too much use. These minor symptoms disappeared after the first 10 days. The arthritis in hand and wrist immediately improved.

Two months after operation this patient fell downstairs again, this time without serious injury. Check-up roentgenograms showed that the screw was pulled about ⅛ inch. New bone formation was visible along the sides of the screw and over its head. Function was not impaired and no pain was experienced. At 4 months this patient still has normal use of her shoulder without symptoms. Roentgenograms (Fig. 4) show an increase in bone formation about the screw.

CASE 2. M. B., aged 73 years, fell from a chair and sustained a complete left acromioclavicular separation with disruption of the coracoclavicular ligament (Fig. 5). Operation was performed in the manner described the evening of the day of injury and the patient went home the next morning. No sling or support of any kind was worn and

the patient was instructed to use the arm as much as possible, within reason. The severe pain was immediately and completely relieved by the operation. At 10 days this patient did up her own hair and dressed herself, even to hat and overcoat, without assistance.

At 3 weeks, while doing heavy lifting, the patient pulled the screw and partial redislocation resulted. At a subsequent operation the screw was replaced. Satisfactory, although not complete, reduction was secured. It is now 7 weeks since the original operation. Position of the bones has been maintained by the screw and she is regaining shoulder function but it is still too early to give a final result in this case.

CASE 3. J. M., aged 65 years, a heavy muscled laborer, was seen in consultation 3 days after a fall which resulted in a complete right acromioclavicular separation. A well applied Velpeau dressing, worn during this interval, had failed to maintain reduction of the dislocation. At operation great difficulty was encountered in replacing the clavicle in its proper relation to the acromion. It was secured with a vitallium screw in a partially reduced position (Fig. 6). Again, no sling or support was worn. He was able to feed and dress himself the day following operation. Within 1 week he had recovered full motion of the arm in all directions. This he has maintained up to the present (6 weeks) but he has not yet been allowed to do any heavy work.

CASE 4. A. M., aged 34 years, a masseuse, fell from a stool and suffered a complete left acromioclavicular separation. Following failure of a pressure dressing to maintain reduction (Fig. 7a), repair was effected with a vitallium screw (Fig. 7b), 2 days after injury. Complete active motion of the arm in all directions was possible immediately at the conclusion of the operation. As a matter of fact her motion was so vigorous that she bent the screw slightly. When seen in the office next day the patient took off and put on her hat, overcoat, and sweater without aid and with no pain or limitation of motion. It is now 5 weeks since her operation. Perfect reduction and function have been maintained but she will not be permitted to resume heavy work for another 2 or 3 weeks.

As a result of the difficulty experienced in Case 3 in reducing the dislocated clavicle and maintaining it in its proper relation to the acromion while the holes were drilled and the screw inserted, I have devised a clavicle depressor (Fig. 8a). With this instrument the tip of the clavicle can easily be moved downward, forward, and medially and held in position by an assistant without his hands encroaching upon the operative field.

While the screw used in these cases has been successful, it is not ideal in that its head is too small, its thread too fine and closely spaced, and its shaft too thin. A special screw with a broader head, a flanged thread, and a slightly heavier shaft has therefore been designed and is now available (Fig. 8b). This provides a better bearing surface on the clavicle as well as a much stronger grip in the coracoid. The head of this screw is not only slotted for the ordinary screw driver but is recessed for use with the patented Phillips screw driver which will not slip out. The screw head is slightly beveled and has a diameter of 7/16 inch. Although the flanged threads of this new screw have a maximum diameter of ¼ inch, the screw can easily be inserted through a 3/16 inch hole in the clavicle due to wide spacing of the threads. The shaft is 5/32 of an inch thick and 1½ inches in length. These measurements were decided upon as the result of careful experimental work on the cadaver.

It is surprising how active and ambitious all these patients have been immediately following the repair. It is difficult to make them realize that they have sustained a serious injury and that they must wait 6 to 8 weeks for scar tissue to reinforce the screw before they attempt any strenuous activity. Since the screw was pulled in Case 2, necessitating a second operation, I have advised against lifting or pulling for at least 6 weeks after operation. This precaution should be observed, I believe, even when the new screw with flanged threads is used, to prevent the threads from pulling through the bone. While the screw itself has been thoroughly tested in the laboratory and found to have a tensile strength of well over 300 pounds upon direct pull, it must be remembered that support really depends upon the strength of the cortical bone until such time as that is reinforced by healing of the ligaments.

SUMMARY

A new method is presented for the repair of acromioclavicular separation, when there is a disruption of the coracoclavicular ligament. This consists of suspending the scapula from the clavicle by a single vitallium screw inserted under local anesthesia, an operation which does not require the patient to be hospitalized. Pain is immediately relieved and function quickly restored since no immobilization or support of the arm is required. This procedure is simple, safe, inexpensive, and immediately effective. Since it is a relatively minor operation, morbidity and mortality are practically eliminated, even in elderly patients, and convalescence is greatly shortened.

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A TEST FOR MEDIAN NERVE FUNCTION

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LESIONS of the median nerve are comparatively common. According to various statistics, during the first World War they ranked next to, or even surpassed, in frequency those of the radial or radial and ulnar nerves. Among the lesions of the median nerve, those affecting the nerve at the wrist or in the palm of the hand are especially common. Here the median nerve is affected most often directly by incisions from contact with broken glass or from suicidal attempts, by falls upon the hand, by fractures of the lower end of the radius, and the like. Also the professional handling of tools that exert pressure on the palm or upon the wrist may affect the median nerve. Lesions of the median nerve located higher up are easy to diagnose since here the flexors of the fingers and of the hand are involved and the vasomotor trophic changes are sometimes very marked. If the nerve is damaged at the wrist, the motor changes affect only the 2½ muscles of the thenar eminence supplied by the median nerve. As the neurological picture may be confused by tendon injuries, the diagnosis of median nerve lesions at the wrist and recognition of their course are at times difficult.

In this article a simple test for median nerve palsy will be described that is equally applicable to median nerve lesions at the wrist and to those higher up, but it is more appropriate for the diagnosis of the former. The only reference to this test I was able to find in the literature is that in the work of Pitres and Testut.[1] The test is so self-evident and simple that it may also have been described elsewhere; yet it is so useful that it deserves detailed description and renewed emphasis.

If the median nerve is damaged at the wrist, the muscles affected are the opponens pollicis, the abductor pollicis brevis, and the superficial head of the flexor pollicis brevis. The cardinal function of these median muscles is the opposition and abduction of the thumb. In testing the function of the median nerve, we are accustomed to examine first of all the opposition of the thumb, but the following circumstances may detract from the value of this test in lesions at the wrist. First, the flexor pollicis longus and the adductor pollicis, to some degree, may substitute for the muscles primarily responsible for opposition of the thumb. Second, the thenar muscles, which participate in the opposition usually innervated by the median nerve, may be innervated to a varying degree by the ulnar nerve. The compensation by other muscles and the innervation of the median muscles by the ulnar nerve explain why in a lesion of the median nerve at the wrist the opposition of the thumb can be performed remarkably well even if the nerve is completely severed. Third, it is sometimes difficult to determine whether there is real opposition (rotation of the thumb around its own axis) so that the tip of the thumb meets the tip of the little finger or whether there is "pseudo-opposition" in which the thumb meets the radial side of the end phalanx of the little finger. In median nerve lesions at the wrist in which the flexor pollicis longus is preserved, this muscle together with the adductors of the thumb (innervated by the ulnar nerve) functions largely in real opposition. Therefore, it would appear *a priori* more advisable in testing the thenar muscles innervated by the median nerve to rely on their function as abductors of the thumb. The ulnar nerve does not participate in the abduction of the thumb. The radial nerve may but it rarely suffers injury together with the median nerve.

This abductor function of the median nerve is too often ignored in textbooks and in monographs on nerve injuries. For example, impairment of the abduction of the thumb as a sign of a median nerve lesion is not even mentioned in the textbook of Bing or in the monographs of Tinel or Stookey.

Our test for a median nerve lesion is performed as follows: The patient is asked to stretch the thumbs of both hands as much as possible, keeping them on a plane with the palm while the other fingers remain adducted. He then is instructed to lift his hands in front of him, as in the position of Oriental prayer, the palms facing the examiner (Fig. 1). In this position the radial tips of the indices touch each other at a horizontal level; so do likewise the tips of both thumbs if there is no lesion of the median nerve. If, however, a median nerve lesion is present, the tip of the thumb of the affected side does not extend horizontally to the tip of the other thumb but instead touches the inner ulnar aspect of the healthy thumb proximal to the tip. The more severe the median nerve palsy is, the more proximally the tip of the affected

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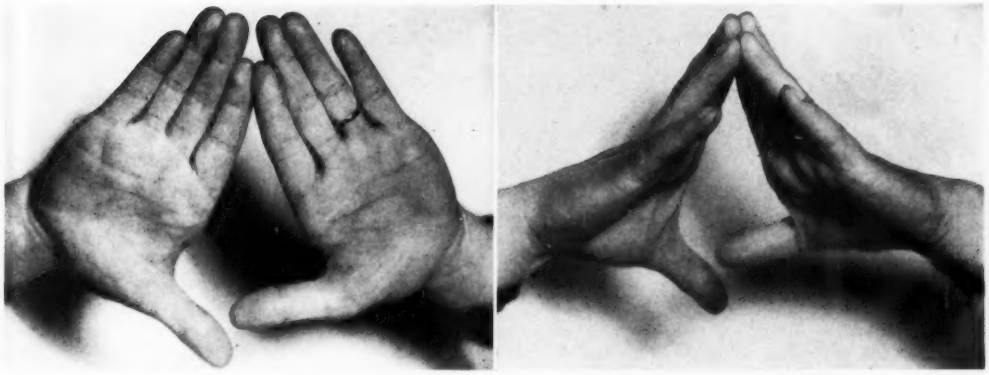
[1] Les nerfs en schémas, p. 388, Paris: Doin, 1925.



Figs. 1 and 2. Median nerve test. Median paralysis on patient's left side. The thumb is held higher than on the healthy side. The more severe the lesion of the median nerve, the higher the position of thumb, and vice versa.

thumb touches the healthy thumb. A subsiding median nerve palsy is characterized by the ability of the patient to reach more nearly the tip of the healthy thumb with the tip of the affected one. One of my patients who had occupational pressure neuritis of the right median nerve discovered this for himself, and at succeeding monthly visits showed me triumphantly how he could more and more nearly reach the tip of the healthy thumb with the tip of the affected one.

Another technique of this test is as follows: The patient brings his inner fingertips together in a rooflike position at such an angle that the tips of the thumbs maximally abducted at right angles to the palms can touch. If median palsy is present, the tip of the thumb on the affected side is horizontally higher due to deficient abduction (Fig. 2).

This modification is a nearly specific test for affections of the median nerve since abduction of the thumb is the domain of this nerve. The radial nerve co-operates in the abduction of the thumb through the abductor pollicis longus muscle, but a simultaneous involvement of the median and radial nerves is unusual. The ulnar nerve is much less likely to participate in abduction than in opposition. Some deny that the abductor pollicis brevis might ever be innervated by the ulnar nerve.

By this test, which is easy to perform and to interpret, the slightest degree of median nerve weakness can be discovered. It is, furthermore, not only a qualitative but also to a certain extent a quantitative test. It is a good test by which to unmask the malingerer, and an appropriate test for demonstration in neurological teaching.

The test proved to be of particular value in cases of palsy of the ulnar muscles in which it is of paramount importance to rule out even the slightest involvement of the muscles innervated by the median nerve. In 3 recently observed cases of atrophy of the ulnar muscles, a concomitant involvement of the median muscles could be clearly demonstrated by this test. Of course, such a finding leads the diagnosis in quite a different direction. The 3 cases mentioned proved to be of the muscular atrophic type and not ulnar nerve paralysis as they seemed to be at first glance.

In median nerve lesions that have been cured by operation or by conservative treatment, the atrophy of the thenar eminence may persist for a long time even after the function of the muscles has become normal. In evaluation of such cases the persistent atrophy may be deceptive because it is muscular function that is most important. The value of the test described lies in the fact that it is a test of function of the muscles supplied by the median nerve. If it is negative, functional recovery is proved despite persistence of some atrophy. This functional restoration can then be confirmed by other tests which show a normal function of median nerve long before the thenar eminence acquires its normal round appearance.

The defective abduction of the thumb in median nerve palsy that constitutes the basis for this test is not easily and clearly evident in the customary examination of a patient with median nerve palsy or by observation of the patient's use of his hands, fingers, or thumbs. Particularly in mild cases, this defective abduction is discernible only by this test in which the patient is made to abduct *ad maximum* his thumb. If the test is negative, i.e., if the tips of the fully abducted thumbs meet at the same horizontal level, it may be concluded that no lesion of median nerve exists, or that complete recovery has ocurred.

DETERMINATION OF PYLORIC PATENCY FOLLOWING THE FREDET-RAMMSTEDT OPERATION FOR CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

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THE Fredet-Rammstedt operation for congenital hypertrophic pyloric stenosis has proved itself one of the most successful procedures in the realm of surgical practice. Donovan's report[1] of 350 consecutive operative cases with one death is evidence of this statement. While many infants are operated upon annually by men who do this operation frequently, still more are probably operated upon by those who do the operation only occasionally. The problem which confronts the occasional operator, as he carries out the technical steps of separating the pyloric musculature, is whether he has actually accomplished relief of the obstruction. He wonders whether he has divided the muscles far enough, he wonders whether the pyloric canal is actually large enough.

Some years ago, as an assistant, I was interested in an infant upon whom the Fredet-Rammstedt procedure was carried out. Following operation, it was evident as time passed that the obstruction had not been sufficiently relieved because the child was still vomiting. Operation was again decided upon and a gastroenterostomy was contemplated. However, when the pylorus was again exposed it was found that the muscles could be separated still further and that the first operation had probably been an incomplete one. In order to avoid such an outcome, in subsequent cases Dr. William A. Fisher suggested making a small incision on the anterior wall of the stomach through which a curved Kelly clamp could be introduced into the pylorus. The jaws of the clamp while in the pyloric canal could be gently spread, giving assurance to the operator that sufficient space was present within the pyloric canal. This maneuver was carried out in a number of cases and worked satisfactorily, especially in convincing the operator that he had attained his original purpose of relieving the pyloric stenosis.

In order to avoid making an incision into the stomach and yet attain the same objective, namely, assurance that the pylorus was patent, it occurred to me that the tip of a catheter which had already been introduced into the stomach through the nose or mouth could be passed through the pyloric outlet. This principle has been employed in a number of cases with very satisfactory results. As a routine, a No. 10 or 12 French catheter is passed into the stomach through the nose following the anesthetization of the infant with ether. This is done in order to insure an empty stomach and to avoid aspiration of gastric contents on the part of the child. When the separation of the pyloric musculature is completed by the usual method of blunt dissection, the operator identifies the catheter by palpating with his thumb and forefinger through the walls of the stomach (Fig. 1). Manipulation of the tube by the anesthesist will often assist him in finding and directing it. When he secures the catheter in his fingers, the catheter of course lying within the lumen of the stomach and the fingers outside, he passes the tip toward the pylorus. The pylorus meanwhile is held with the fingers of the left hand and with the right hand the tip is directed into and through the pyloric canal. If the tip passes through into the duodenum, the operator can be assured that the pylorus is patent. The catheter can then be partially or completely withdrawn from the stomach depending upon the desires of the operator. In a few instances some difficulty was experienced in finding and manipulating the tube, but usually this was accomplished with ease.

The objection may be raised that this procedure is wholly unnecessary because so many successful cases have been reported without it. The answer to this objection is that the method gives the operator assurance that he has gained his objective, an assurance which he can scarcely have in any other way. If the catheter fails to pass, he can proceed at once to bring about a wider separation of the muscles thereby allowing more space through which the catheter may then be passed. In using this method there has been no evidence of danger, and the soft catheter can hardly be expected to tear the overlying mucosa. Its tip

[1] Donovan, E. J. Congenital Hypertrophic Pyloric Stenosis, Practice of Surgery, by Lewis. Vol. 6, chap. 7, p. 5. Hagerstown, Md.: W. F. Prior Co., 1910.

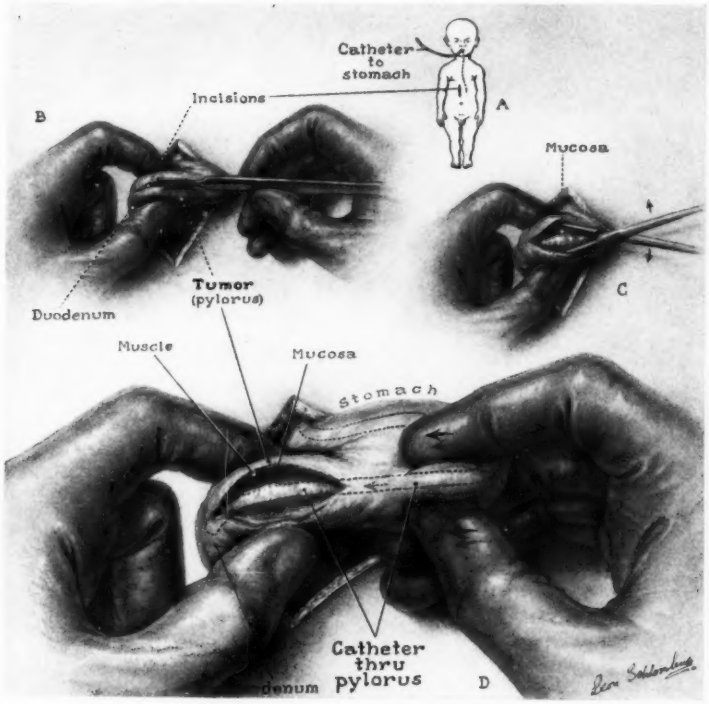

Fig. 1. Method of passing catheter through pyloric canal to determine its patency following the Fredet-Rammstedt procedure.

can readily be seen as it passes, outlined by the mucous membrane. There has never been any suggestion of damage. The method proved especially helpful in 2 cases in which the duodenum had been inadvertently opened at the distal end of the pyloric wound. This accident which happens occasionally is readily remedied by closing the serosa with fine sutures of silk at the point where minute gas bubbles are seen to emerge. In order to be certain that the closure had not caused constriction, the catheter was passed into the duodenum in each of these cases. This was evidence enough to convince me that the lumen was still sufficient.

This procedure has been used to supplement the Fredet-Rammstedt operation in 8 patients operated upon either by the resident surgeons or myself at the Union Memorial Hospital during the past 3 years. All of the infants have done well and the maneuver suggested here has been considered to be of definite value in the satisfactory completion of the operation.

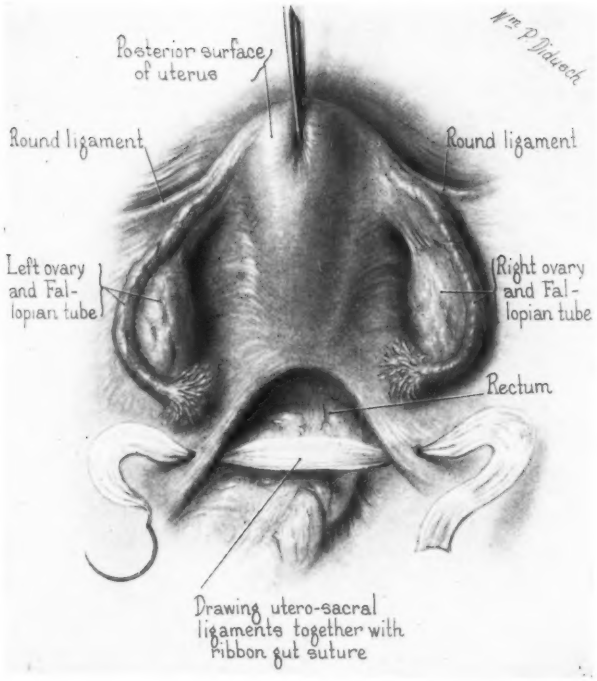

Fig. 1. The uterus has been delivered at the abdominal wound. The uterosacral ligaments are drawn together with a ribbon-gut suture studded at one end with an atraumatic needle.

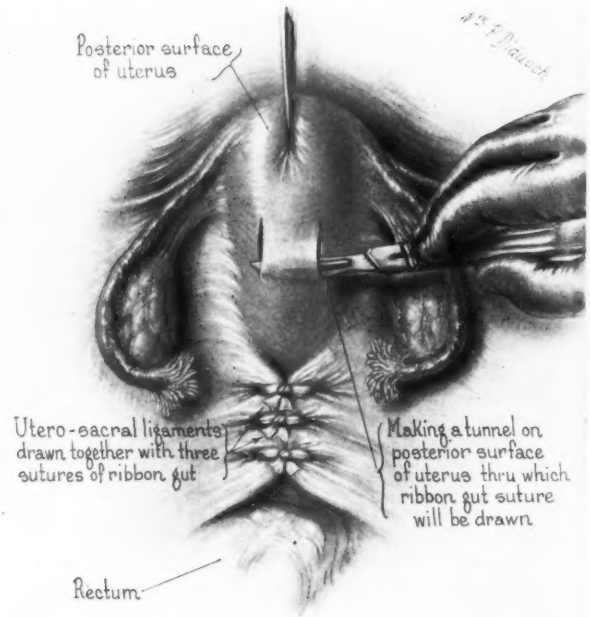
Posterior surface of uterus
Utero-sacral ligaments drawn together with three sutures of ribbon gut
Making a tunnel on posterior surface of uterus thru which ribbon gut suture will be drawn
Rectum

Fig. 2. The uterosacral ligaments are snugly drawn together with 3 sutures of ribbon gut. A tunnel is made on the posterior surface of the fundus uteri through which a ribbon-gut suture will be drawn.

Use of Ribbon Gut in Uterine Suspensions.—Daniel Chanis, Jr.

USE OF RIBBON GUT IN UTERINE SUSPENSIONS

DANIEL CHANIS, Jr., M.B., Ch.B. (Edin.), Panama, Panama

RETRODISPLACEMENT of the uterus is a condition so frequently submitted to surgical intervention, and one for which there are so many methods of correction, that the surgeon often finds himself confronted with the problem of deciding which is the best technique to follow.

Recent considerations of the problem of uterine displacements have impressed gynecologists with the importance of judging each case upon its merits rather than adhering, routinely, to a particular operative technique. As Crossen aptly remarks: "Most of the symptoms in retrodisplacements are due to complicated conditions. These complications must be recognized and treated if the symptoms are to be relieved. The complications determine to a very large extent the method of treatment to be employed for the displacement."

In those cases of retrodisplacement in which a future pregnancy is possible and the adnexa of both sides are intact and the tissues freely mov-

From the Urological Service, Santo Tomás Hospital, Panama.

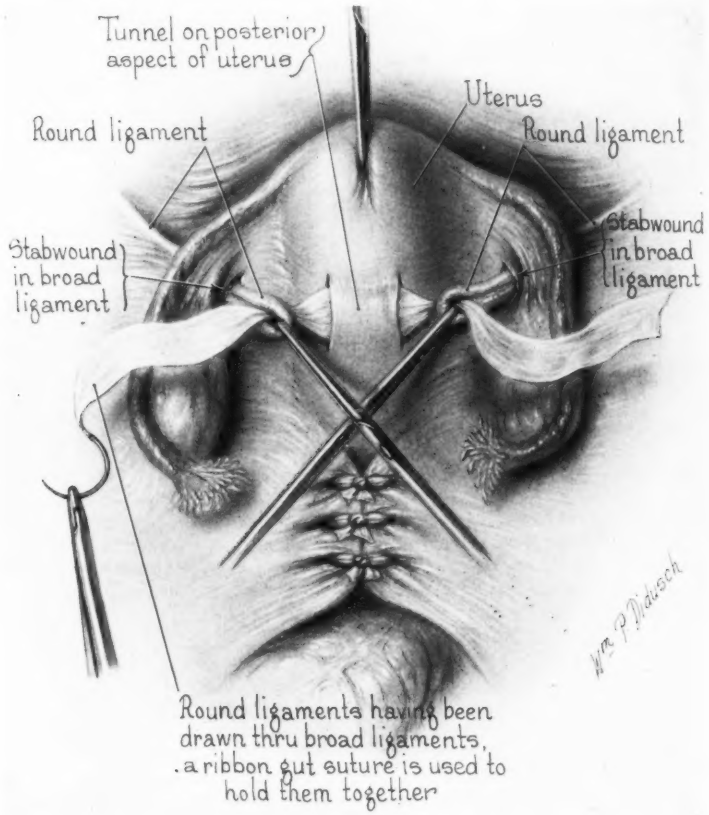
Tunnel on posterior aspect of uterus
Uterus
Round ligament
Round ligament
Stabwound in broad ligament
Stabwound in broad ligament
Round ligaments having been drawn thru broad ligaments, a ribbon gut suture is used to hold them together

Fig. 3. The round ligaments having been drawn through the broad ligaments, a ribbon-gut suture is drawn through one round ligament, carried through the tunnel, and then through the round ligament on the opposite side.

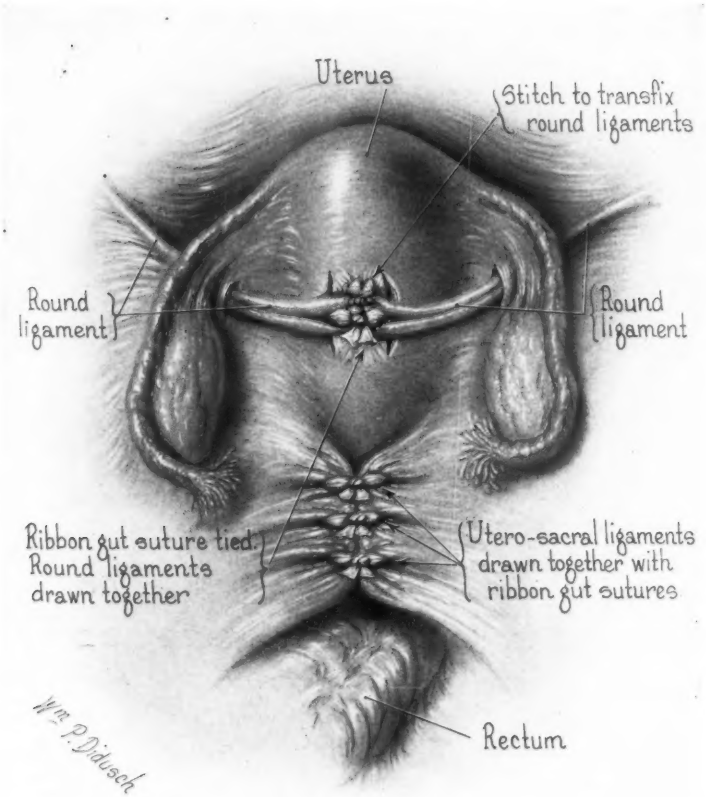

Fig. 4. The ribbon-gut suture is tied, and the round ligaments brought together. An extra suture of ribbon gut is placed so as to transfix the round ligaments and the peritoneal covering of the uterus overlying the tunnel.

able, the "posterior implantation of the round ligaments" has been widely used with good results.

The experimental work of O. S. Lowsley (2) on dogs, in which he used chromic ribbon gut in nephropexies, has shown that this material is invaded by fibroblasts which build a strong fibrous tissue bridge on the ribbon. This fact has led Lowsley and his co-workers to use ribbon gut not only in kidney operations but also in other fields of surgery when a sound, strong plastic repair is needed—perineal prostatectomy (3), operations for hernia (1) perineal operations, etc. (4, 5, 6). In all of these procedures, ribbon gut has proved highly efficient, and its employment has marked a distinct advance in surgical technique.

The efficiency of ribbon gut in other branches of surgery suggested its use in the operation of "posterior implantation of the round ligaments" in uterine displacements. It was felt that it would give better support and stronger anchorage to the uterus than are achieved by the use of ordinary catgut or silk.

TECHNIQUE OF OPERATION

At the Santo Tomás Hospital, we have been employing the following technique, in those cases in which the uterus is free and movable and the adnexa intact.

The uterus having been delivered at the abdominal wound, the uterosacral ligaments are snugly brought together over the posterior aspect of the uterocervical segment by two or three sutures of chromic ribbon gut studded at one end with an atraumatic needle (Figs. 1 and 2).

With a sharp knife, a tunnel is made on the posterior aspect of the fundus uteri. The round ligaments having been drawn through the broad ligaments, one is transfixed by the ribbon gut, which is carried through the tunnel to the opposite round ligament and tied (Fig. 3). An extra suture of ribbon gut is placed so as to transfix the round ligaments and the peritoneal covering of the uterus overlying the tunnel (Fig. 4).

RESULTS

It is too early to draw definite conclusions regarding the real value of this technique in maintaining the uterus in position, especially after subsequent pregnancies; but it is hoped, and believed, that better results can be expected from the use of ribbon gut than have been obtained by the employment of other suture material.

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THE EFFECT OF DISTENTION UPON WHOLE BLOOD SPECIFIC GRAVITY AND WHOLE BLOOD POTASSIUM

SAMUEL B. CHILDS, M.D., and JOHN SCUDDER, M.D., F.A.C.S.,
New York, New York

THE importance of the rôle played by distention as a factor in the morbidity and mortality of acute intestinal obstruction has recently become increasingly appreciated by both clinical and experimental workers. It is a recognized surgical principle today, that in small intestinal obstruction, decompression of bowel lumen proximal to the site of obstruction, together with a restoration of fluid nitrogen and electrolyte balance, is of the greatest importance.

In a recent review Leigh, Nelson and Swenson were able to show that with the use of the Miller-Abbott tube as an adjunct to surgery of small intestinal obstructions, a mortality of 5.9 per cent was obtained in 68 cases in which the tube was employed, as opposed to previous mortality figures from the same hospital ranging from 66.6 per cent (1916–1919) to 27.6 per cent (1932–1935).

In the voluminous work upon experimental intestinal obstruction, the rôle of distention has received significant comment only during the past decade. Cooper in a comprehensive review of the literature, does not bring up the question of distention *per se*, although he raises 40 pertinent questions in regard to intestinal obstruction.

Herrin and Meek point out that while in 1933 "a toxemia is still generally regarded as the cause of all symptoms, a small group has dissented from this view and presented experimental evidence to show that death from high intestinal obstruction is probably due to non-toxic factors such as dehydration, decrease in blood volume, loss of electrolytes, loss of something specific in the gastrointestinal secretions or alkalosis."

Working with Thiry and Thiry-Vella fistulous loops of the upper jejunum in dogs, they found that "constant distention of the loops with from 50 to 80 millimeters of mercury results in malaise, loss of appetite, excessive secretion from the loops, desiccation and dechlorination of tissues, decreased blood and plasma volumes, increased hemoglobin content, moderately increased alkali reserve, high nonprotein nitrogen and greatly decreased blood chloride."

From the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University.

They felt that the initiating cause of the whole train of symptoms might be the distention of an intestinal segment, and that the loss of chloride was the most serious sequela.

Taylor, Weld, and Harrison stated that "if distention is the primary cause of the sequence of events seen in obstruction, then distention alone should produce the same results as an actual mechanical obstruction." With this hypothesis, they utilized a distensible balloon fashioned around a noncollapsible rubber tube, so that the continuity of the lumen through the distended loop was not eliminated. They found that "most of the animals in which the pressure employed was around 100 millimeters of mercury died within 24 hours with the usual symptoms and postmortem findings of acute obstruction." They observed a close relationship between the severity of symptoms and the degree of distention. They found that in animals which died within 40 hours there was no significant fall in chloride.

They concluded that "distention of the bowel wall is the important factor in the production of the symptoms of experimental intestinal obstruction" and suggested that reflex disturbances effected by afferent nerve stimulation were possibly the significant factor in the train of events.

Fine, Rosenfeld and Gendel, employing the entire ligated small intestine of the cat, to which the extrinsic nerve supply had been eliminated, found that the survival time of the animals was inversely proportioned to the level of pressure in the lumen of the bowel, and that such exclusion of the extrinsic nerve supply did not alter the survival time.

Gendel and Fine, employing the entire small intestine of the dog, found that obstructed dogs which were distended, died more rapidly than simply obstructed dogs, and found that distention of the intestine had a deleterious effect on the general circulation. In distended, obstructed dogs they found an early and progressive loss in plasma volume from 36.4 per cent in 4 to 6 hours to 55 per cent in 24 hours. In this paper as in others they point out that distention *per se* does not effect a significant loss of fluid into the lumen of the gut.

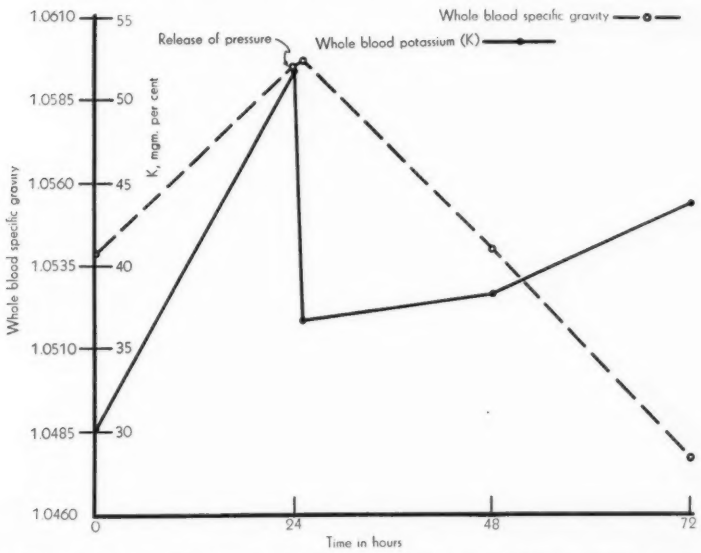

Chart 1. Cat 25. Distention—obstruction without strangulation; pressure, 30 millimeters mercury.

The work cited is in accord with the history that distention greatly aggravates and accelerates, if it is not *per se*, the lethal factor in intestinal obstruction. The modus operandi is not clear. Taylor, Weld, and Harrison did not find chloride loss an early phenomenon. Fine, Rosenfeld, and Gendel found that denervated intestine behaved as did the innervated bowel. Gendel and Fine found a significant loss of plasma volume in distended obstructed intestines in dogs.

Scudder, Zwemer, and Truszowski (7) obstructed the lumen of the intestine of the cat, with tape, at various levels, and followed the condition of the animal to its lethal termination, with frequent determinations of whole blood potassium and whole blood specific gravity. They found a fluctuating rise in blood potassium to lethal levels, which was preceded by a rise in the blood density.

Many workers have pointed out the analogy in symptoms and signs in such critical conditions as adrenal insufficiency, shock, intestinal obstruction, intestinal fistulas. Scudder (6) has reported blood studies in these conditions and has pointed out the value of determinations of blood density as of value in the guide to therapy.

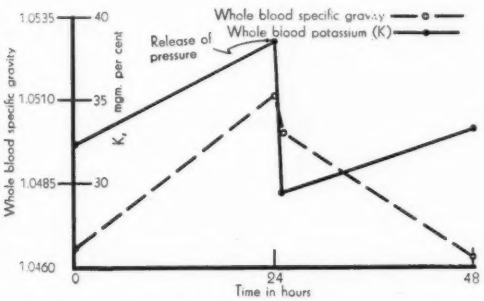

Chart 2. Cat 23. Distention—obstruction without strangulation; pressure, 30 millimeters mercury.

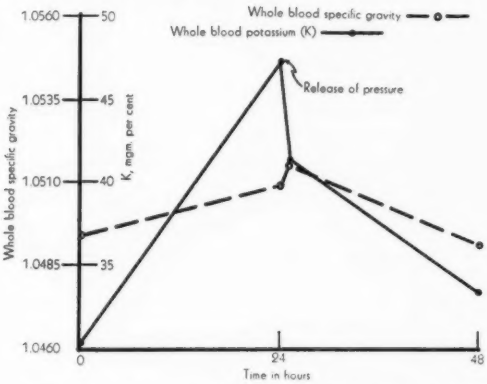

Chart 3. Cat 24. Obstruction—distention without strangulation; pressure, 30 millimeters mercury.

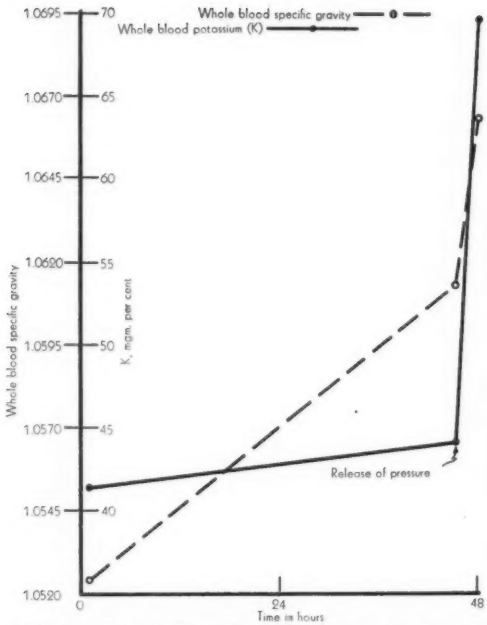

Chart 4. Cat 21. Distention—obstruction with strangulation; pressure, 44 millimeters mercury.

In the following experiment the distending pressure was interrupted after varying intervals and concomitant values of whole blood specific gravity and whole blood potassium were recorded. An evaluation of the method of potassium determination with the reservations necessary to its use is discussed by Scudder (6).

Preliminary experiments were carried out on 17 cats to ascertain an effective means of introducing a Miller-Abbott tube into the lumen of the intestine of the cat, to ascertain the most effective distending pressure, which could be used in the balloon, without compromising the blood supply of the wall with subsequent necrosis and perforation, and in determining the effects of this type of distention-obstruction on the bowel of cats.

METHOD

The distending medium used was a 16 centimeter condom rubber balloon attached to a No. 14 double lumen rubber tube, similar to the Miller-Abbott (1934) tube. The balloon was introduced through a small opening in the stomach to the desired level in the duodenum, below the ampulla of Vater, the stomach and abdominal wounds were closed around the tube, and the cat was allowed to recover from the ether anesthesia.

It is appreciated that when such a balloon is distended, there is associated obstruction of the lumen of the intestine. The obvious advantage of the method lies in the facility with which the distending pressure may be released, without a second laparotomy.

The cats were fasted for a preliminary 24 hours, so that the small intestine was empty and collapsed. Blood samples were taken from the ear for simultaneous whole blood specific gravity and whole blood potassium determinations, and argenti cobaltonitrite method used for potassium (6).

Blood was taken before anesthesia, 24 hours after distention, 1 hour after release of distention, and 24 hours after release of distention.

When the animal was wide awake after the cessation of ether anesthesia, the balloon was inflated to a pressure of 30 millimeters of mercury. This was accomplished by displacing air from a bottle by the induction of water via a tube from another bottle raised to the height requisite (39 cm.) to register 30 millimeters of mercury pressure on an attached manometer. By using leak proof tested apparatus, the maximum drop in pressure during the duration of the experiments was 1 centimeter of water level.

The distending pressure was then employed for 24 hours, second readings taken, and the pressure released. After one hour a third set of readings was obtained, and 24 hours later a fourth set.

The cats under these conditions suffered the effects of distention and obstruction as witnessed by their appearance of malaise and discomfort, and by the vomiting of bile-stained duodenal contents. They were given no water nor parenteral fluid during this time.

Charts 1, 2, 3 illustrate the changes in the values of blood potassium and whole blood specific gravity which accompanied distention of the lumen of the duodenum of the cat by the method described. The distending pressure was maintained for 24 hours, and then released. In these instances, at the end of 24 hours of distention there was a marked elevation of whole blood potassium and a similar marked rise in the whole blood specific gravity. An hour after the release of the distending pressure there was an appreciable fall of whole blood potassium toward the base level, and a subsequent fall in whole blood specific gravity. At autopsy, when the animals were killed, no compromised loops of bowel were found.

Charts 4 and 5 show the changes in two cats in which the distending pressure was higher, 44 millimeters of mercury, and in which the pressure was maintained for 48 hours. At the end of 48

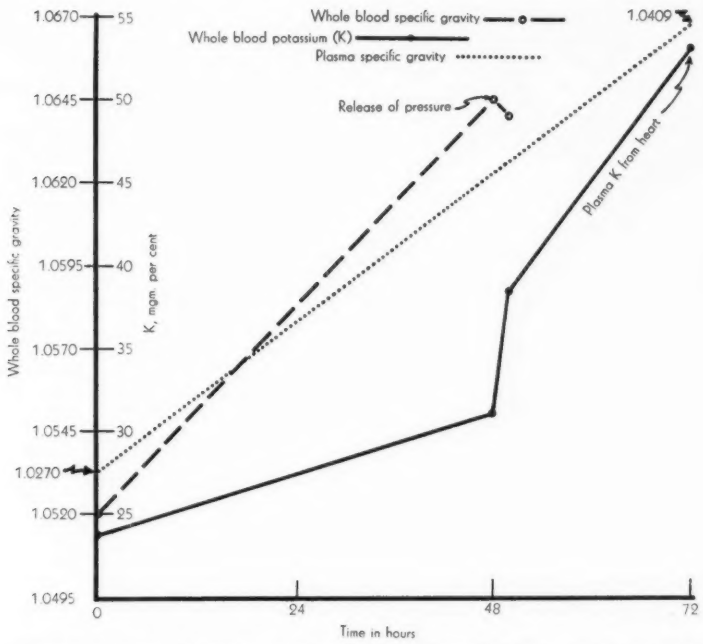

Chart 5. Cat 20. Distention—obstruction with strangulation; pressure, 44 millimeters mercury.

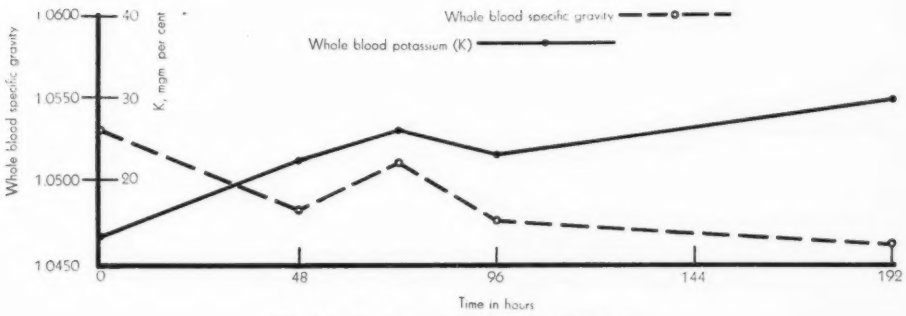

Chart 6. Control cat. Balloon not inflated.

hours there was an elevation in whole blood potassium and a marked elevation of whole blood specific gravity. An hour following release of the pressure there was instead of a fall of these values (Chart 4) a striking rise, as shown. The animal died 1½ hours after the release of pressure and a gangrenous loop of duodenum was found.

Chart 5 shows the same rise in potassium after 1 hour and a transient drop in whole blood specific gravity. The subsequent rise at the end of 72 hours is shown. The animal died at 72 hours and a gangrenous loop of duodenum was found.

Chart 6 illustrates the values in a cat in which the balloon was introduced but not inflated.

CONCLUSIONS

Following 24 hours of distention of the duodenum of the cat there is an elevation of peripheral whole blood potassium and whole blood specific gravity.

One hour following release of the distending pressure, there is a fall in whole blood potassium and at the end of 24 hours following release of distention there is a continued fall in potassium and a fall in whole blood specific gravity. These values are recorded in animals without fluids.

Following 48 hours of distention with a higher pressure there is an observable rise in both of these values.

Following the release of the distending pressure for such a time, the combination of which is sufficient to produce a gangrenous loop, the values abruptly rise to the lethal termination.

In the first instance, i.e., in distention of short duration without compromise of bowel, the process is reversible; in the second, i.e., the longer period of distention with compromise of bowel, the release of the distending pressure is accompanied by an increase in the hemoconcentration and rise in potassium.

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BILE AS A THERAPEUTIC AGENT

THE elaboration of bile is an important function of the liver and constitutes an essential factor for normal digestion. Bile salts are prepared solely in the liver. There has been ample proof that the synthesis of bile salts is interfered with following obstruction of the common duct. Suppression of bile salt formation rapidly follows after obstruction to the outflow of bile and returns to normal only after a long period of time. Digestive disturbances associated with gall-bladder disease are difficult to evaluate as regards the initiating factors, but there is good presumptive evidence that deficiency of bile salt in the bile of patients with diseases of the extrahepatic bile ducts is in a large measure responsible. Winfield has shown definite improvement as regards anorexia and flatulence in a majority of cases of cholecystitis after whole bile administration. The use of whole bile or bile salts after release of common duct obstruction has provided additional evidence of the efficacy of this material. Analysis of common duct drainage bile not only indicates the deficiency of bile salts but affords proof that the bile salt content of bile can be replenished by the administration of dried animal bile or by bile salts. Not only is the oral administration efficacious as simple substitutive therapy during the phase when no bile may be entering the duodenum, but bile salt is rapidly and efficiently absorbed and excreted. Reabsorption and reexcretion of bile salt affords an efficient means of conserving this material. Accordingly, the bile as excreted may be brought back to normal constituency and thus the difficulties associated with the qualitative and quantitative deficiency of bile corrected. While there is specificity as regards the type of bile salt in various animals, there seems to be no specificity as regards the ability of one animal effectively to use the bile of another.

Bile preparations in therapy, especially for digestive disorders, have long been popular. There has been a tendency toward the use of extracts of bile such as extract of fel bovis, or preparations consisting of some fraction of bile either alone or mixed with other agents, especially cathartics. The ineffectiveness of these preparations as substitutes for bile led to the troublesome task of reintroducing the bile drained from choledochostomy tubes back into the patient by stomach tube.

The availability of effective bile preparations affords relief from the distasteful task of introducing the patient's own bile by stomach tube in cases draining from a choledochostomy. This practice at best was not too efficacious since the bile introduced in this way was often devoid of bile salt. The more pleas-

ant method of administering concentrated bile or purified bile salt is more effective, since adequate concentrations of bile salts are assured. It is usual for patients with severe disease of the extrahepatic biliary tract to have a deficiency of bile salt in the bile, and it is wise to supplement this. In addition, the added choleresis resulting tends to aid in flushing out the common duct and decreases the amount of sediment found.

Bile salt or whole bile administered to patients with gall stones is palliative treatment and cannot be relied upon for permanent relief. As an adjunct to surgery, bile therapy is important before operation to help in restoring or maintaining an adequate prothrombin level and in adding to the comfort of the patient. After operation, restoration of bile salt in the patient's own bile by the administration of bile from animals affords a physiological means of restoring to normal the disturbed digestive processes resulting from deficiency in the patient's own bile.

CHARLES G. JOHNSTON.

BLOOD PLASMA PROTEINS

POINTS of view relative to plasma proteins have been changing rapidly during the past 10 years. It is fair to say that 20 years ago physicians looked upon the plasma proteins as inert materials having to do with osmotic pressure but not concerned with the internal protein metabolism of the body. Many believed that they could be replaced adequately by inert materials such as gums, for example, acacia.

Experimental work has brought many facts to light which indicate that the physician must know more about plasma proteins. Their importance in the next few years will probably increase rather than diminish and their study will be of corresponding interest to surgeons and physicians. Much research work with animals and careful study of clinical cases are being published, and this trend undoubtedly will increase.

It is our belief that the plasma proteins take an active part in the internal protein metabolism of the body, that they are built up rapidly, used in the body economy freely, and serve to supply practically all of the protein requirements of the cells of the body. Evidence is at hand to show that a healthy dog can produce a maximum of about 1 gram of plasma protein per kilogram body weight per day, and it is probable that the human being under favorable circumstances can do something of the same order. This means that a 10 kilogram dog can produce 10 grams of new plasma protein a day, which amounts to about a third of his circulating plasma protein, a turn-over, let us say, of 30 per cent being a distinct possibility.

A dog may be maintained in nitrogen equilibrium, weight equilibrium, and in health by injecting protein in suitable amounts as dog plasma while feeding only fat, carbohydrate, salts and accessories. This plasma protein given by vein obviously supplies all the requirements of the healthy animal over periods of many weeks. If this can be done in such an emergency, it probably is done more or less continuously in health. It seems likely that this plasma protein supplies the protein requirements of the various cells of the body, organs, muscle, and interstitial tissue. Many of the plasma proteins are believed to be formed in the liver, although a few of the globulins undoubtedly are formed outside of the liver. The liver, therefore, is the great factory which produces this actively metabolized protein for use throughout the body.

There are many occasions when use of plasma protein concerns the surgeon and physician. Any form of hypoproteinemia may

be tested and many cases of shock of all types are now being treated with plasma protein given as whole plasma. It is obvious that a study of the ways and means by which the body builds new plasma protein is of great interest in connection with these shock problems. Probably the introduced plasma protein not only serves to adjust osmotic pressures but furnishes needed protein material for repair and replacement of injured cells. The body builds this type of protein from food protein, but fortunately has *in reserve* considerable amounts of material stored in the body from which it can build plasma proteins rapidly in an emergency. When this reserve store is depleted, new plasma proteins depend almost wholly on incoming food protein. In this emergency the healthy animal can use almost any type of food protein, but the animal proteins in general are better utilized than the vegetable and grain proteins.

It is reasonable to study whether amino acids and various protein digests can be used to facilitate this rebuilding of plasma protein. A considerable variety of digests and foreign proteins have been tested. Large protein molecules have a tendency to give trouble because of sensitization but they have usefulness and are being studied. Digests in which amino acids and polypeptides predominate are well utilized to form new plasma protein, under experimental conditions. So far as tested in this laboratory, *casein digests* seem to be most effective. If properly prepared it is not necessary to supplement these digests with amino acids. Amino acids are being tested alone, and combined in various mixtures. In this way in emergencies it may be possible to supplement or even to replace considerable amounts of plasma protein with digests out of which the body can make promptly its own new plasma proteins.

This work with protein digests calls for a wide variety of animal experiments and cautious, controlled tests on selected human cases. Such work is in progress in various laboratories and hospitals, and will prove to be of much interest in the coming years. It should be helpful to the physician to think of plasma proteins not as an inert matrix but as a part of the great body protein pool. It is obvious that there is a ready exchange (dynamic equilibrium) between the proteins of the cells of the body and the plasma proteins. In emergencies these cells can contribute materials out of which plasma protein is promptly made, presumably in the liver. During periods of plenty the body stores away large reserves which can be drawn on in emergencies. Depletion of these *protein reserves* is dangerous not only from the standpoint of the plasma protein in circulation but because these depleted individuals are so easily injured by drugs, by infection, and probably by a wide variety of injurious agents as compared with the normal controls. G. H. WHIPPLE.

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REVIEWS OF NEW BOOKS

A BRITISH text *A Pratical Manual of Diseases of the Chest*[1] first appearing in 1935, is now in its second (1941) edition. The material has been extensively revised and the chapter bibliographies contain many recent references.

This treatise reports in a practical, didactic fashion both the medical and surgical aspects of most of the chest disease problems encountered.

The introductory 4 chapters of the volume consider a fundamental study of the anatomy, physiology, radiology and physical diagnosis related to the respiratory system. The 32 remaining chapters are devoted to a clinical review of most of the common and rare chest diseases. These are included in groups divided by clinico-anatomical regions as follows: diseases of the upper respiratory tract—nasopharyngitis, laryngitis; diseases of the lower respiratory tract—bronchitis, bronchiectasis, foreign bodies; asthma; pleural diseases; diseases of the lung—collapse, emphysema, pneumonia—37 pages; tuberculosis—124 pages; intrathoracic suppuration; new growths; and miscellaneous—differential diagnosis, mediastinal disease, oxygen therapy, prescription formulary.

The presentations are well illustrated by numerous clear x-ray reproductions, charts, photomicrographs, and drawings; there are about 200 such. Sixty-two well chosen case histories from the files of the Brompton Hospital are cited to portray the practical clinical problems.

As is to be expected in a volume by a single author, much more emphasis is placed on certain disease entities than others. The author in writing of diseases with which he is less familiar has obtained the best opinion presented in available literature and presents his conclusions on these phases.

The major respiratory disease problems are efficiently treated. This manual is a valuable asset to the library of the student of medicine, as a text for the undergraduate or a reference work for the busy practitioner.

EUGENE L. WALSH.

THE comparatively brief book *The Pharmacology of Anesthetic Drugs; A Syllabus for Students and Clinicians*[2] by John Adriani presents by means of diagrams, schematic drawings and tables, a digest of the properties, actions, and techniques of administration of the anesthetic agents, both for general anesthesia and local anesthesia, as well as of various auxiliary agents. The method of presentation is therefore not well suited to casual reading, but would probably be of value as a teaching manual in a course devoted to anesthetics. The title of the book might be interpreted by many clinicians to signify that it is primarily devoted to the basic and fundamental problems of anesthesia and anesthetic agents. This is not the case, as it is most concerned with the items of interest to the practicing anesthetist and surgeon. The method of presentation necessitates a rather dogmatic treatment, but the author has been as judicious in this respect as the method would permit.

CARL A. DRAGSTEDT.

THE book of Samson Wright on *Applied Physiology*[3] has represented an outstanding contribution to texts in the field of physiology since the first edition. This seventh edition represents a marked improvement. So much new material has been added that practically every chapter has been enlarged and improved. Practically every advance made in physiology in recent years, of importance to the physician and to the student of medicine, is included. The book unquestionably exemplifies the importance of physiology in the practice of medicine and how the recognition of this fact has grown in recent years. The book is recommended to students and practitioners of medicine without reservation.

A. C. IVY.

THE third volume of the four-volume work on therapeutics edited by Blumer[4] with a number of contributors has recently appeared. The material covered includes diseases due to fungi, metazoan and protozoan diseases, intoxications, diseases due to physical agents, treatment of edema, dehydration, acidosis and alkalosis, preoperative and postoperative treatment, treatment of diseases of the lower respiratory tract, treatment of diseases of the blood and lymph vessels, and treatment of heart disease.

This volume continues to present in a stellar manner the basic underlying treatment. In fact the work improves with each succeeding volume. As in previous sections there is some duplication. For instance scorpion poisoning is described in two chapters, incidentally with disagreement as to the production of scorpion antivenin.

[1] A PRACTICAL MANUAL OF DISEASES OF THE CHEST. By Maurice Davidson, M.A., M.D. (Oxon.), F.R.C.P. (Lond.). 2d ed. London and New York: Oxford University Press, 1941.

[2] THE PHARMACOLOGY OF ANESTHETIC DRUGS; A SYLLABUS FOR STUDENTS AND CLINICIANS. By John Adriani, M.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

[3] APPLIED PHYSIOLOGY. By Samson Wright, M.D., F.R.C.P. 7th ed. New York: Oxford University Press, 1940.

[4] THE THERAPEUTICS OF INTERNAL DISEASES. Edited by George Blumer, M.A. (Yale), M.D. With the assistance of Albert J. Sullivan, M.D. Vol. 3. New York and London: D. Appleton-Century Co., Inc., 1941.

Contributors continue to be prominent specialists well qualified in the various fields. Particularly noteworthy are chapters by the senior author on intoxications, treatment of diseases of the blood and lymph vessels by Wright, and treatment of heart disease and heart failure by Marvin. While titled *The Therapeutics of Internal Diseases*, this work is developing into an excellent treatise on medicine with special emphasis on treatment.

JAMES R. MILLER.

SINCE its first edition in 1915 *First Aid in Emergencies*[1] by Eldridge L. Eliason has enjoyed wide distribution. This 260 page, pocket-size book is designed for police, firemen, boy scouts, and many other lay groups. The tenth edition has been completely revised and reset and illustrated with 126 halftone and line drawings. Resetting has been typographically satisfactory but the revision has not rejuvenated an aging volume. For example, the author recommends the use of laudanum or lead water, or both, to laymen for such widely varying conditions as contusions, insect wounds, sprains, dislocations, fractures, corrosive acid poisoning, asthma, earache, and hives; and apparently does not realize that no layman is able to purchase laudanum legally within the United States since it is subject to the rules and regulations of the Narcotic Act.

His recommendations in the treatment of dislocations by laymen are open to question. For example in the treatment of dislocation of the shoulder the directions state: "Send for a physician. If one is not obtainable, then you may try reduction." Then he describes for the layman the hazardous technique used in the Hippocratic period of placing the foot in the axilla with progressive traction on the arm, and erroneously refers to Figure 50. At no point is there any caution of possible fracture-dislocation or damage to axillary vessels and nerves. Under dislocation of the elbow in describing the deformity and illustrating it, the author states "Reduction is usually left to a physician" and then describes how it should be done showing a halftone illustration of a husky, shirt-sleeved individual reducing an elbow fracture across the knee after the method described by Sir Astley Cooper.

In describing "carriage in supine position" the description states all three bearers kneel, each on one knee (the knee nearest the patient's feet) and then shows two illustrations showing all three bearers kneeling on the knee nearest the patient's head.

An undesirable illustration shows the obsolete technique of elevation of a patient's pelvis for "emptying water from the lungs." This technique has long been discontinued as it is inadequate and delays the beginning of revivification procedures.

Under foreign bodies of the eye, among the directions to laymen are, "If the particle is easily seen and a physician is not available, gentle attempts may be made to dislodge it with a sterile needle point. A drop of 1 per cent cocaine solution in the eye one minute before attempting removal helps." These directions are for laymen.

The woefully incomplete index which presumably would be used in emergency does have an entry for botulism but no entry for food poisoning; no entry under bites; no entry under dog or dog bites—yet it does index Gila monster. There are many similar but perhaps minor criticisms that might be added.

This handy volume, bound in a semiflexible water resistant cover, contains many interesting descriptions and illustrations but could be recommended only to the highly critical reader and certainly not to the average inexperienced novice who wishes to be helpful in an emergency. FELIX JANSEY.

[1] FIRST AID IN EMERGENCIES. By Eldridge L. Eliason, A.B., M.D. Sc.D., F.A.C.S. 10th ed. Philadelphia, Montreal, and London: J. B Lippincott Co., 1941.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

INFANTILE PARALYSIS; A SYMPOSIUM DELIVERED AT VANDERBILT UNIVERSITY, APRIL, 1941. New York: The National Foundation for Infantile Paralysis, Inc., 1941.

THE PRINCIPAL NERVOUS PATHWAYS; NEUROLOGICAL CHARTS AND SCHEMAS WITH EXPLANATORY NOTES. By Andrew Theodore Rasmussen, Ph.D. 2d ed. New York: The Macmillan Co., 1941.

ÉTUDES SUR LES AMPUTATIONS ET DÉSARTICULATIONS DES MEMBRES. By P. Huard. Paris: Masson & Cie., 1940.

CLINICAL AND EXPERIMENTAL INVESTIGATIONS ON THE GENITAL FUNCTIONS AND THEIR HORMONAL REGULATION. By Bernhard Zondek. Baltimore: The Williams & Wilkins Co., 1941.

MEDICAL PROGRESS ANNUAL, 1940; REPORTS PUBLISHED DURING 1940 IN THE NEW ENGLAND JOURNAL OF MEDICINE. Edited by Robert N. Nye, M.D. Baltimore, Md., and Springfield, Ill.: Charles C. Thomas, 1941.

TRABAJOS DE LA CÁTEDRA DE SEMIOLOGÍA QUIRÚRGICA. By Manuel Riveros M. Buenos Aires: Nocito & Ranó, 1941.

RECUPERACIÓN QUIRÚRGICO-ORTOPÉDICA DE LOS MUTILADOS DE GUERRA. Madrid: Sanidad Militar, 1941.

ELECTROCARDIOGRAPHY; INCLUDING AN ATLAS OF ELECTROCARDIOGRAMS. By Louis N. Katz, A.B., M.D. Philadelphia: Lea & Febiger, 1941.

EXERCISES IN ELECTROCARDIOGRAPHIC INTERPRETATION. By Louis N. Katz, A.B., M.D. Philadelphia: Lea & Febiger, 1941.

ABDOMINAL SURGERY OF INFANCY AND CHILDHOOD. By William E. Ladd, M.D., F.A.C.S., and Robert E. Gross, M.D. Philadelphia: W. B. Saunders Co., 1941.

LYMPHATICS, LYMPH, AND LYMPHOID TISSUE; THEIR PHYSIOLOGICAL AND CLINICAL SIGNIFICANCE. By Cecil Kent Drinker, M.D., D.Sc., and Joseph Mendel Yoffey, M.Sc., M.D., F.R.C.S. (Eng.). Cambridge, Massachusetts: Harvard University Press, 1941.

THE COMPLETE WEIGHT REDUCER. By C. J. Gerling. New York: Harvest House, 1941.

THE CARE OF THE AGED (GERIATRICS). By Malford W. Thewlis, M.D. 3d ed. St. Louis: The C. V. Mosby Co., 1941.

OPERATIVE SURGERY; INCLUDING ANESTHESIA, PRE- AND POSTOPERATIVE TREATMENT, PRINCIPLES OF SURGICAL TECHNIC, BLOOD TRANSFUSION AND ABDOMINAL SURGERY. Edited by Frederic W. Bancroft, A.B., M.D., F.A.C.S. New York and London: D. Appleton-Century Co., Inc., 1941.

NECROPSY; A GUIDE FOR STUDENTS OF ANATOMIC PATHOLOGY. By Béla Halpert, M.D. St. Louis: The C. V. Mosby Co., 1941.

BODY MECHANICS IN HEALTH AND DISEASE. By Joel E. Goldthwait, M.D., F.A.C.S., LL.D., Lloyd T. Brown, M.D., F.A.C.S., Loring T. Swaim, M.D., and John G. Kuhns, M.D., F.A.C.S. With a Chapter on the Heart and Circulation as Related to Body Mechanics. By William J. Kerr, M.D., F.A.C.P. 3d ed. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1941.

CLINICAL IMMUNOLOGY, BIOTHERAPY AND CHEMOTHERAPY IN THE DIAGNOSIS, PREVENTION AND TREATMENT OF DISEASE. By John A. Kolmer, M.S., M.D., Dr. P.H., Sc.D., LL.D., L.H.D., F.A.C.P., and Louis Tuft, M.D. Philadelphia and London: W. B. Saunders Co., 1941.

SURGICAL DISEASES OF THE SPINAL CORD, MEMBRANES, AND NERVE ROOTS; SYMPTOMS, DIAGNOSIS, AND TREATMENT. By Charles A. Elsberg, M.D., with chapters by Cornelius G. Dyke, M.D., and Abner Wolf, M.D. New York: Paul B. Hoeber, Inc., 1941.

THE THERAPEUTICS OF INTERNAL DISEASES. Edited by George Blumer, M.A. (Yale), M.D., and Albert J. Sullivan, M.D. Vol. 4 and Vol. 5. New York and London: D. Appleton-Century Co., Inc., 1941.

THE HEALTH AND EFFICIENCY OF MUNITION WORKERS. By H. M. Vernon, M.A., M.D. London: Humphrey Milford (Oxford University Press), 1940.

SULFANILAMIDE AND RELATED COMPOUNDS IN GENERAL PRACTICE. By Wesley W. Spink, M.D. Chicago: The Year Book Publishers, Inc., 1941.

SURGERY OF HEAD AND NECK (Oxford Medical Outline Series). By Arthur S. McQuillan, A.B., M.D., F.A.C.S. London, Toronto, and New York: Oxford University Press, 1941.

THORACIC SURGERY (Oxford Medical Outline Series). By Charles W. Lester, A.B., M.D., F.A.C.S. London, Toronto, and New York: Oxford University Press, 1941.

ABDOMINAL SURGERY (Oxford Medical Outline Series). By John E. Hammett, M.D., F.A.C.S. London, Toronto, and New York: Oxford University Press, 1941.

FRACTURES AND DISLOCATIONS (Oxford Medical Outline Series). By Kenneth M. Lewis, B.S., M.D., F.A.C.S. London, Toronto, and New York: Oxford University Press, 1941.

VISUAL OUTLINE OF PSYCHIATRY (Oxford Medical Outline Series). By Leland E. Hinsie, M.D. London, Toronto, and New York: Oxford University Press, 1941.

HISTOLOGY AND EMBRYOLOGY (Oxford Medical Outline Series). By José F. Nonidez, Sc.D. London, Toronto, and New York: Oxford University Press, 1941.

DISEASES OF THE RESPIRATORY TRACT (Oxford Medical Outline Series). By Jacob Segal, M.D., F.A.C.P., F.A.C.C.P., with a foreword by Harry Wessler, M.D. London, Toronto, and New York, 1941.

OBSTETRICS (Oxford Medical Outline Series). By Hervey Clock Williamson, M.D., F.A.C.S., and George Schaefer, M.D. London, Toronto, and New York, 1941.

THE EARLY TREATMENT OF WAR WOUNDS (Oxford War Manuals). By William Anderson, O.B.E. (Mil.), M.B., Ch.B., F.R.C.S. London: Oxford University Press, 1941.

THE FOOT AND ANKLE; THEIR INJURIES, DISEASES, DEFORMITIES AND DISABILITIES; WITH SPECIAL APPLICATION TO MILITARY PRACTICE. 2d ed. By Philip Lewin, M.D., F.A.C.S. Philadelphia: Lea & Febiger, 1941.

A TEXT-BOOK OF PATHOLOGY. Edited by E. T. Bell, M.D. 4th ed. Philadelphia: Lea & Febiger, 1941.

ESSENTIALS OF GENERAL SURGERY. By Wallace P. Ritchie, M.D. St. Louis: The C. V. Mosby Co., 1941.

ANALGESIA OBSTÉTRICA; EL SUEÑO CREPUSCULAR BARBITÚRICO EN EL PARTO; CON ESTUDIO ESPECIAL DEL PENTOBARBITAL SÓDICO. By Juan Leon. Buenos Aires: El Ateneo, 1941.

THE BAKER MEMORIAL; A STUDY OF THE FIRST TEN YEARS OF A UNIT FOR PEOPLE OF MODERATE MEANS AT THE MASSACHUSETTS GENERAL HOSPITAL. By Haven Emerson, M.D. New York: The Commonwealth Fund, 1941.

OM CYSTOMETRI HOS PROSTATIKERE; MED SPECIELT HENBLIK PAA METODENS KLINISKE BETYDNING. By Olaf Povlsen. Copenhagen: Ejnar Munksgaard, 1941.

MOTHER AND BABY CARE IN PICTURES. By Louise Zabriskie, R.N. 2d ed. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1941.

WOUNDS AND FRACTURES; A CLINICAL GUIDE TO CIVIL AND MILITARY PRACTICE. By H. Winnett Orr, M.D., F.A.C.S. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1941.

DISEASES OF THE THYROID GLAND; PRESENTING THE EXPERIENCE OF MORE THAN FORTY YEARS. By Arthur E. Hertzler, M.D. New York and London: Paul B. Hoeber, Inc., 1941.

THE PREMATURE INFANT; ITS MEDICAL AND NURSING CARE. By Julius H. Hess, M.D., and Evelyn C. Lundeen, R.N. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1941.

THE TREATMENT OF BURNS. By A. B. Wallace, M.B., F.R.C.S. Ed., M.Sc. (McGill). London: Humphrey Milford (Oxford University Press), 1941.

TECHNIQUE OF GASTRIC OPERATIONS. By Rodney Maingot, F.R.C.S. Eng. London: Oxford University Press, 1941.

A MANUAL OF THE TREATMENT OF FRACTURES. By John A. Caldwell, M.D. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1941.

SYNOPSIS OF THE PREPARATION AND AFTERCARE OF SURGICAL PATIENTS. By Hugh C. Ilgenfritz, A.B., M.D., and Rawley M. Penick, Jr., Ph.B., M.D., F.A.C.S., with a foreword by Urban Maes, M.D., D.Sc., F.A.C.S. St. Louis: The C. V. Mosby Co., 1941.

SURGERY OF THE HEART. By E. S. J. King, M.D., M.S., D.Sc. (Melb.), F.R.C.S. (Eng.), F.R.A.C.S., Major A.A.M.C. Baltimore: The Williams & Wilkins Co., 1941.

THE 1941 YEAR BOOK OF RADIOLOGY. DIAGNOSIS edited by Charles A. Waters, M.D., and Whitmer B. Firor, M.D. THERAPEUTICS edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1941.

DISEASES OF THE BLOOD AND ATLAS OF HEMATOLOGY; WITH CLINICAL AND HEMATOLOGIC DESCRIPTIONS OF THE BLOOD DISEASES INCLUDING A SECTION ON TECHNIC AND TERMINOLOGY. By Roy R. Kracke, M.D. 2d ed. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1941.

CANCER OF THE FACE AND MOUTH; DIAGNOSIS, TREATMENT, SURGICAL REPAIR. By Vilray P. Blair, M.D., Sherwood Moore, M.D., and Louis T. Byars, M.D. St. Louis: The C. V. Mosby Co., 1941.

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